STUDIES OF REPRODUCTIVE HEALTH AMONG CHILDBEARING AGE WOMEN IN RURAL SOUTH INDIA

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Submitted to the Graduate Faculty of

the Graduate School of Public Health in partial fulfillment

of the requirements for the degree of

Doctor of Philosophy

University of Pittsburgh

2013

UNIVERSITY OF PITTSBURGH

GRADUATE SCHOOL OF PUBLIC HEALTH

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April 15, 2013

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ABSTRACT

Reproductive conditions and adverse birth outcomes disproportionately affect women in developing countries. Despite this fact, most research has been conducted with women in the United States and Europe. We sought to determine the burden and risk factors for reproductive outcomes among the 1,226 South Indian women in the Longitudinal Indian Family Health (LIFE) study.

Bacterial vaginosis (BV) affected 14.1% (95% confidence interval (CI) 11.9-16.4%) of women in LIFE. When diagnosis by clue cells alone was compared to Nugent's scoring, clue cell analysis had a sensitivity of 39.8% (95% CI 36.6-43.0%) and specificity of 81.2% (95% CI 78.6-83.8%), with higher sensitivity among non-pregnant women (41.5%; 95% CI 37.8-45.2%) compared to pregnant women (29.4%; 95% CI 22.9-35.9%). Use of clue cells alone for diagnosis was found to be inadequate for screening women for BV and a validated method is recommended for future practice.

We investigated several potential risk factors to determine their association with BV. In the model adjusted for religion and water source, Muslim women were more likely to have BV compared to Hindu women, though the increase was not significant (adjusted odds ratio (OR_{adj}) 1.8; 95% CI 0.9-3.6). Women using tap water were also more likely to have BV at baseline

compared to those who used purchased water (OR_{adj} 1.4; 95% CI 0.9-2.0), though this increase was also not significant. These potentially at risk groups should be targeted for future screening programs.

Consanguineous marriage (CM) occurs in up to 46% of South Indian marriages. Among women in CMs, we found a significant increase in the risk of early ($\leq$10 weeks' gestation) spontaneous abortion (SAB) (adjusted hazards ratio (HR_{adj}) 2.7, 95% CI 1.1-7.0). There was also a trend toward an increase in risk of late SAB (11-22 weeks' gestation) (HR_{adj} 1.2, 95% CI 0.4-3.7) and all SAB (HR_{adj} 1.9, 95% CI 0.9-3.8). Women in CMs should be identified by health care providers and given counseling prior to conception and throughout pregnancy.

This dissertation yields public health significance by identifying high-risk groups who should be targeted for screening and counseling programs by the clinics serving this rural South Indian population.

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PREFACE

This collaboration would not have been successful had it not been for the individuals at both MediCiti Institute of Medical Sciences and the University of Pittsburgh. My special thanks goes to Maggie Whelan, Ravi Patel, Tushar Singh, Kalpana Basany, Sastry Gurumurthy, Aparna Varma, Mumatha and Deepa.

1.0 SPECIFIC AIMS

Adverse gynecologic and obstetric outcomes, including vaginal infections, spontaneous abortion, low-birth weight, intrauterine growth restriction, and preterm birth, account for a significant amount of maternal and infant morbidity worldwide.[1-3] This burden is disproportionally placed on developing countries. Despite this, few research studies have focused their efforts on identifying specific risk factors in these populations. The overall goal of this study is to determine the causes of adverse gynecologic and reproductive outcomes among women living in rural Andhra Pradesh, India.

Bacterial vaginosis (BV) affects up to 39% of women in India. [4, 5] Transmission and risk factors for BV are poorly understood and may vary based on characteristics of the population being studied. Untreated, BV can lead to serious reproductive morbidity, including endometritis [6-9], cervicitis [8, 10-12], and pelvic inflammatory disease. [13-17] Among pregnant women, BV has been associated with spontaneous abortion, preterm birth, and low birth weight. [7, 11, 18-20] However, data on the association between BV and these outcomes is mixed. Proper screening tests for BV play a critical role in ensuring that women are diagnosed correctly and that treatment can be provided in a timely manner.

Consanguineous marriages, especially among first cousins, are common in India. In the Indian state of Andhra Pradesh, population based surveys estimate the prevalence as 46%.[21] Consanguinity has been associated with increased risk of infant morbidity and mortality,

including excessive infant deaths, stillbirth, congenital malformations, and rare genetic conditions. [22-26] Studies of pregnancy outcomes from consanguineous marriage have largely been conducted in Middle Eastern countries and few investigations have focused on India. Outcomes may vary between populations based on the amount of genetic mixing and consanguinity.[27] This study aims to examine these risk factors in order to provide information to health care providers and researchers that will help to alleviate the heavy burden of adverse reproductive outcomes in rural Andhra Pradesh.

The Longitudinal Indian Family Health (LIFE) Study is a longitudinal study in rural Andhra Pradesh, India, near the city of Hyderabad. Women and their husbands are recruited prior to conception or in the early weeks of pregnancy and followed through conception, pregnancy, delivery, and the postpartum period. Infants are followed through the first year of life. The focus of the study is to determine the risk factors leading to the high rates of adverse pregnancy outcomes, including spontaneous abortion, birth of a low birth weight or intrauterine growth restricted infant, preterm birth, and chorioamnionitis.

A major innovation and strength of the LIFE study is that the Indian population studied attempts conceptions soon after marriage and has limited use of contraceptives. This allows us to enroll couples and measure risk factors pre-pregnancy. Due to limitations of identifying early pregnancies and biases involved in enrolling only women in a planning population, this study will provide a unique perspective and allow for testing of a variety of factors that have otherwise been unstudied.

To this end, this dissertation seeks to achieve the following goals:

1. To determine the reliability of using clue cells as a test for bacterial vaginosis compared to using Nugent's criteria**.** *We hypothesize that using clue cells alone will have poor sensitivity and specificity compared to Nugent's criteria.*
2. To determine the population-based prevalence of and risk factors for bacterial vaginosis in rural Andhra Pradesh. *We hypothesize that women with BV at registration will be more likely to belong to a lower caste, report douching, report previous vaginal infections, report a recent urinary tract infection, and use tap water.*
3. To determine the association between consanguinity and spontaneous abortion in rural Andhra Pradesh. *We hypothesize that women in consanguineous marriages will have an increased risk of spontaneous abortion.*

2.0 BACKGROUND AND SIGNIFICANCE

2.1 BACTERIAL VAGINOSIS

Bacterial vaginosis (BV) is characterized by a change in the normal vaginal flora from a majority of lactobacilli to a mix of anaerobes, *Gardnerella vaginalis,* and *Mycoplasma hominis.*[28] In a healthy vagina, the lactobacilli are responsible for producing hydrogen peroxide (H_2O_2), which acts as an antimicrobial and prevents the overgrowth of other bacteria. [28] Among women of childbearing age, BV is the most common vaginal infection, with prevalence estimates ranging from 5% in extremely low-risk population [29] to 73% in high-risk populations recruited from sexually transmitted infection (STI) clinics. [30] In the general population, most studies have found a prevalence of about 20% to 40%.[31-34] Symptoms include abnormal vaginal discharge, abnormal odor, and burning or itching. The majority of women, up to 85%, do not report experiencing any of these symptoms. [35]

The exact etiology of BV is currently unknown. While *G. vaginalis* was originally implicated as the organism responsible for this condition, later studies have shown that BV is a polymicrobial condition that has no one single causative agent. [28, 36, 37] *G. vaginalis* remains an important organism in the development and diagnosis of BV, with studies reporting that 50% to 100% of women with BV found to have *G. vaginalis* in their vaginal flora. [37-41] While the detection of *G. vaginalis* has been found to be 90% to 100% specific for diagnosis of BV,

specificity estimates range from 40% to 97%, with most studies showing numbers on the lower end. [37, 39-41] *G. vaginalis* is also found in up to 60% of women with normal and intermediate vaginal flora. [37, 39, 41] This evidence demonstrates the need for more research into the various organisms associated with the development of BV and the role each of them plays in determining outcomes. Unlike sexually transmitted infections (STIs), reproductive tract infections like BV are influenced by behavioral factors such as douching[42-44], smoking[45-47], and stress[48] and socio-demographic risk factors such as race[49-51] and social class. [50, 52] More research is needed to understand the transmission, development, and treatment of BV.

BV is a serious women's health concern as it has been associated with a number of adverse outcomes. Among non-pregnant women, BV has been associated with the development of pelvic inflammatory disease (PID) [13-17], cervicitis [8, 10-12], and infertility.[16, 53-55] BV infection may also make women more vulnerable to sexually transmitted infections, including Chlamydia, gonorrhea, and human immunodeficiency virus (HIV). [56-60] Among pregnant women, BV has been associated with an increased risk of spontaneous abortion (SAB), preterm birth (PTB), low birth weight (LBW), and chorioamnionitis. [7, 11, 18, 19] These adverse outcomes demonstrate the need for timely screening, diagnosis, and treatment of women with BV, in addition to identification and reduction of modifiable risk factors associated with infection.

2.1.1 Diagnosis of BV

2.1.1.1 Clinical Diagnostic Methods

More than 80% of women with BV are asymptomatic. [32] Even among symptomatic patients, signs are nonspecific and easily confused with other vaginal infections. Symptoms include thin,

white or grey discharge with or without a fishy odor, burning during urination, and itching around the outside of the vagina. [61] Many women mistakenly self-diagnose as a yeast infection and treat with over-the-counter medications that are ineffective for the treatment of BV. In physician offices, diagnostic tests are used to differentiate BV from other common vaginal infections.

In clinical practice Amsel's Criteria is most often used for diagnostic purposes. Diagnosis is made if a woman meets three of the four following criteria: 1) vaginal pH >4.5, 2) clue cells present on >20% of cells, 3) positive whiff test, and 4) abnormal discharge.[62] Though attempts have been made to develop an accurate screening tool such as a questionnaire or screening kit [63-65], that can be used by either the patient or a provider to ascertain BV without a full clinical evaluation, none have proven sensitive or specific enough for routine use. This presents an ongoing problem for diagnosis since many clinicians do not follow a full set of diagnostic criteria, which may result in up to 50% of cases being missed.[66]

2.1.1.2 Standard Laboratory Methods

In research, BV diagnosis is typically done through microscopic examination of a slide made from a vaginal swab. This method was first proposed in the early 1920s by Schöder, who identified three different grades of vaginal flora seen on a wet mount slide.[67] Grade I describes specimens showing numerous, normal lactobacillary morphotypes without other bacteria. Grade IIa describes specimens with mostly normal lactobacillary morphotypes, but where other bacteria are also seen. Grade IIb defines specimens where lactobacillary morphotypes are seen but are outnumbered by other coccid bacteria. Grade III is considered Grade III, where few to no lactobacillary morphotypes are seen and have been replaced by coarse, coccid bacterial or numerous parabasal epithelial cells. [68] This method was later rearticulated by Donders in a

paper comparing the Lactobacillary grades to diagnoses made using Amsel's and Nugent's methods. While a number of similarities exist, the Grades described above do not correspond directly to categories created by these other diagnostic systems.[68] Spiegel et al. described a similar method of diagnosis using Gram stain slides instead of wet mounts. Using a system of scoring, each morphotypes was quantified as 1+ when there was <1 morphotypes per field, 2+ where there was one to five per field, 3+ when there were six to 30 per field, and 4+ when more than 30 were present. [69] Based on this system, when only *Lactobacillus* morphotype was present (3 to 4+) or was present with only the *Gardnerella* morphotype (1 to 2+), the slide is interpreted as normal. When the flora is mixed and the Gardnerella morphotype and other bacteria where present and *Lactobacillus* was not present or only present in low numbers (1 to 2+), the slide is classified as consistent with BV.[69] This system was later updated and modified by Hay et al. to include an intermediate category. Thus, the normal classification described above became Grade I, which described a flora made up of predominately Lactobacillus morphotypes. An intermediate level (Grade II) was added, describing those with reduced lactobacillus morphotypes mixed with other morphotypes. Finally, the category consistent with BV, termed grade III, was reserved for those with few or no lactobacillus and an increased number of Gardnerella morphotypes and/or other morphotype.[70] Currently, the scoring system described by Nugent et al. is considered to be the gold standard for diagnosis in research settings[71] This method involves examining Gram-stained slides for the presence and of three types of morphotypes: lactobacillus morphotypes, Gardnerella and *Bacteroides* spp. morphotypes, and *Mobiluncus* spp. morphotypes (Table 1). Overall scores of zero to three are considered normal, scores of four to six intermediate, and scores of seven to ten are considered to be consistent with BV.

The use of Nugent's criteria for diagnosing BV has been examined extensively and found to have a high degree of sensitivity (89.1%) and specificity (83.1%) compared to Amsel's clinical criteria.[72] In addition, studies have shown that the method has a high degree of inter-reader reliability, with kappa scores ranging from 0.62 to 0.75, indicating a high level of agreement. [73-75] While extremely useful for diagnosing BV, Nugent's criteria requires both a longer period of time from testing to diagnosis and trained lab staff capable of reading and scoring the slides properly.

Table 1. Nugent's scoring method for diagnosing BV

Score	Lactobacillus morphotypes	*Gardnerella* and *Bacteroides* spp. morphotypes	Curved gram-variable rods (*Mobiluncus* spp. morphotypes)
0	≥30	0	0
1	5-30	<1	<1
2	1-4	1-4	1-4
3	<1	5-30	5-30
4	0	≥30	≥30

Normal: 0-3; Intermediate: 4-6; BV: 7-10

2.1.1.3 Use of Polymerase Chain Reaction

BV is not well understood. In recent years, polymerase chain reaction (PCR) methods have been developed and used to study the fastidious and difficult to culture bacteria associated with BV. Since multiple microorganisms are involved in the development of BV, specific knowledge of individual organisms may help to identify women with infections that put them at higher risk of adverse outcomes. Colonization of the vagina by lactobacillus species is important for the prevention of BV as many of these species produce hydrogen peroxide which is detrimental to the growth of BV pathogens. A handful of studies have sought to investigate the predominate species of lactobacillus in healthy women. A study of 23 healthy Swedish women showed that the most commonly occurring species, in descending order of frequency, to be *L. crispatus, L. gasseri, L. iners,* and *L. jensenii*. [76] These results are similar to what was previously reported by another group, who identified *L. crispatus, L. iners, L. jensenii,* and *L. gasseri* as the most common species in a group of American women. [77] One hypothesis for the differences in species found is based on previous research on the colonization of the intestinal tract by lactobacillus species which has shown great variety dependent on geographic location. A study of women in Nigeria showed similar results to the studies of white women, with the most common species of lactobacillus being *L. iners, L. gasseri, L. plantarum,* and *L. crispatus*. [78] Other possible explanations for the differences in species found among different groups of women may be related to testing variables, particularly for members of the *L. acidophilus* complex, where phenotypic criteria are unreliable. [76]

Identifying the most common species of lactobacillus provides important information about the etiology of BV. This knowledge may be most beneficial when looking at adverse outcomes, including recurrent infection, preterm birth, and chorioamnionitis. Wilks and

colleagues found that different species of lactobacillus produce different amounts of hydrogen peroxide. [79] As this mechanism is what helps prevent the growth of BV-associated bacteria, those colonized with high H_2O_2 producing species may be less likely to develop BV or have recurring infections. This same study found that women who had vaginal colonies of *L. jensenii* and *L. vaginalis*, the two species with the highest levels of H_2O_2 production, had half the risk of preterm birth and/or chorioamnionitis compared to those colonized with other species. [79]

PCR has also been used to identify the bacteria associated with BV infection. These methods are necessary and important because many species of bacteria associated with BV, such as Gardnerella and Mobiluncus, are also found in women with normal vaginal flora. [37] Specifically, the method has shed light on the polymicrobial nature of the condition. Studies have shown that while women without BV have a vaginal flora almost completely dominated by species of Lactobacillus, women with BV have a large variety of vaginal bacteria. Oakley et al. were able to observe 61 taxa among infected women; however, due to the limitations of identification, they estimate that the true number they identified is closer to 75 (95% CI 63-111). [80] Studies have demonstrated that certain bacteria found to be highly associated with BV may provide more specific and sensitive diagnoses than currently practice. Most useful, appear to be BVAB1, BVAB2, BVAB3, *Gardnerella*, *Atopobium* species, *Eggerthella*-like uncultured bacteria, *Leptotrichia* species, and *Megaspherea α.* [37] In particular, compared to Amsel's criteria, BVAB2 provided 88.9% sensitivity and 95.7% specificity, *Eggerthella*-like uncultured bacteria provided 92.6% sensitivity and 91.3% specificity, and *Leptotrichia* species provided 85.2% sensitivity and 95.7% specificity. When BVAB2 and *Megaspherea α* were combined, sensitivity was 100.0% and specificity 91.3%. [37] These values are in contrast to the normally cited *Gardnerella*, which was shown in this study to have 100.0% sensitivity but only 41.3%

specificity. [37] A second study by the same group found that detection of either a *Megaspherea* species of a Clostridiales bacteria had a sensitivity of 99% and specificity of 89% for compared to Amsel's and 95.9% sensitivity and 93.7% specificity compared to Nugent criteria. [36] Again, G. vaginalis was shown to be highly specific compared to Amsel's and Nugent, 96.3% and 97.3% respectively, but not specific, 29.5% and 45.5%. [36] Another important finding from PCR is that while many fastidious bacteria, such as *L. sanguinegens/amnionii*, *A. vaginae*, and BVAB1, are associated with BV as defined by Amsel and Nugent; they were not associated with abnormal vaginal discharge. [81] These results indicate that certain organisms may be associated with specific symptoms. Importantly, this may provide a reason why many women remain asymptomatic.

2.1.1.4 Diagnosis using Self-Collected Vaginal Swabs

For many reasons, individuals may not be able to attend a clinic or hospital in order to be screened for BV. This is especially true in resource poor settings or rural areas where providers are few and far between. For the purposes of research studies, the use of self-collected vaginal swabs allows more women to be screened in a shorter period than would be allowed if a provider was required to collect each sample. While only a few studies have compared the ability of self-collected vaginal swabs to diagnose BV compared to provider-collected vaginal swabs, the results are strikingly swayed toward their reliability.

In a study of 84 pregnant women from an obstetrics ward in South Africa, Sturm et al. found between 86% and 90% agreement in the results from self-collected tampon fluid and provider collected swabs for diagnosis of BV using Nugent criteria, depending on the observer.[82] Nelson et al. examined self- and provider-collected vaginal samples from forty-three women presenting for a prenatal visit at less than twelve weeks' gestation at the Hospital of

the University of Pennsylvania. For the comparison of self- versus provider-collected swabs, they found strong validity for a dichotomous diagnosis, with a kappa value of 0.94 ($p<0.001$), and for the continuous Nugent score ($r=0.83$).[83] Tanksale et al. examined self- and provider-collected vaginal swabs for BV by Nugent score among 75 pregnant, non-pregnant, and postpartum women attending an outpatient gynecology clinic in India and found high agreement, with a kappa of 0.98 ($p<0.001$).[84] Strauss et al., examined the concordance of BV status by Nugent score made from self- and provider-collected vaginal swab among 129 women 24 to 29 weeks' gestation seeking care at a University of North Carolina Hospital. The authors found that, when compared to the provider-collected swab, the self-collected swab had a sensitivity of 77%, specificity of 97%, positive predictive value of 71%, negative predictive value of 97%, and a kappa of 0.71 (95% CI: 0.51-0.91). In addition, when compared across the three grade levels, there was substantial agreement between the self- and provider collected sample, with a weighted kappa of 0.82 (95% CI: 0.72-0.91).[85] Kashyap et al. examined self- and provider-collected samples for BV using Nugent scores for 50 women attending an outpatient gynecology clinic in India and found moderate agreement between the two collection methods (kappa=0.48). The ability of the self-collected sample to determine BV had a sensitivity of 70%, specificity of 97%, positive predictive value of 94% and a negative predictive value of 83%. Overall, the predictive value of the self-collected swab was 86%.[86]

Overall, these studies provide sufficient evidence that using self-collected vaginal swabs for the detection of BV by Nugent’s criteria is both accurate and sensitive. In situations where it is inconvenient or prohibitively expensive to have provider-collected samples, self-collected vaginal swabs are an appropriate substitution.

2.1.2 Treatment of BV

A woman's vaginal flora can differ greatly over a relatively short period of time.[87] In studies of spontaneous recovery, 13% to 50% of women went from BV by Nugent's criteria to either abnormal or normal flora within a period of one month from original testing.[88, 89] While many women with BV recover spontaneously, treatment for all symptomatic women and asymptomatic non-pregnant women is recommended by the Centers for Disease Control and Prevention (CDC) in order to prevent complications.[90] Standard treatment regimens are typically very successful when used as directed with most courses showing cure rates of at least 70%.[91, 92] However, many patients either fail to respond to treatment of suffer from frequent relapses. Studies have shown that up to 70% of patients have a recurring infection within a year of the initial treatment[91, 93], with most studies showing rates closer to 30%. [94-96] Alternative therapies are often recommended in these instances, as well as an assessment of possible behavioral modifications.[90]

2.1.2.1 Among Non-Pregnant Women

Based on an assessment of the woman's preferences, allergies, and drug interactions, standard treatment involves a course of 500 mg of Metronidazole taken orally twice a day for seven days, use of five grams of 0.75% Metronidazole gel intravaginally once a day for five days, or use of five grams of 2% Clindamycin cream intravaginally for seven days. Other possible treatments include the use of one and two gram oral doses of Tinidazole and a shortened use of 100 mg Clindamycin ovules intravaginally for three days.[90]

As previously stated, the above regimens are not always efficacious. Development of alternative treatment methods has yielded numerous hypotheses and potential drugs, but none

which have shown significant results. The research with the most potential relates to the use of probiotics as a way to cure BV. Since BV results from an overgrowth of bacteria following the loss of normally occurring Lactobacillus, it is hypothesized that the reintroduction of these morphotypes may improve treatment outcomes. Of the four major studies published to date, half have shown statistically significant results. [97-100] The first study examined the use of oral probiotics in addition to oral metronidazole and found an overall small, but statistically significant, odds of having a normal Nugent score following treatment for those receiving probiotics (OR: 0.09; 95% CI: 0.03-0.26).[97] Another study comparing the use of intravaginal probiotics to a placebo and found the intervention to group to be more likely to clear the infection than the control group (OR: 0.02; 95% CI: 0.00-0.47).[100]

The remaining studies were unable to show significant results using intravaginal probiotic therapies. A study by Anukam et al., comparing intravaginal probiotics with metronidazole found a non-significant increase in the odds of having a normal Nugent score following the intervention treatment (OR: 0.27; 95% CI: 0.07-1.10).[98] Eriksson et al., compared the use of vaginal clindamycin with vaginal showed the opposite effect of other studies, with those in the placebo group being more likely to have normal Nugent scores than those in the experimental group (OR: 1.21; 95% 0.67-2.19).[99] Overall, evidence supporting the use of probiotics is weak. Further research needs to be done to determine the best strains to introduce to the vaginal flora of individuals and determine the appropriate drug regimens to accompany their use.

2.1.2.2 Among Pregnant Women

The United States Preventive Services Task Force (USPSTF) recommends against screening for BV among asymptomatic pregnant women, regardless of their risk for adverse pregnancy outcomes.[101] The main basis for their decision is that there is insufficient evidence that treatment of asymptomatic BV in pregnant women decreases the risk of outcomes such as preterm birth. Some evidence even points to the fact that the treatment itself may have serious consequences, greater than those caused by the infection. [102-107]

Multiple studies have been done to look at whether screening and treatment of BV during pregnancy reduced the risk of preterm delivery. The majority of these studies have found either no difference between the preterm birth rate among those randomized to treatment and control. A few studies have shown a significant increase in risk among those receiving treatment.

The most commonly examined drug is vaginal clindamycin. In a study of single uterine pregnancies among women with no prior preterm births, 101 women who screened positive for BV by gram stain at approximately 12 weeks' gestation were randomized to receive either 20mg/g clindamycin cream or a placebo for one week. Participants were rescreened one week after treatment and again at 30 weeks' gestation. A total of 10 women in the study had a preterm birth, 7 from the group treated with clindamycin (13.7%) and 3 from the group treated with a placebo (6.0%). Overall, the researchers found a non-significant increase in the risk of preterm birth among women who screen positive for BV and were treated compared to women who screen positive but received a placebo (OR: 2.1; 95% CI: 0.6-10.0). [102] In another study by Kekki et al., the authors looked at women who screened positive for BV by gram stain between 10 and 17 weeks' gestation. A total of 375 women were randomized to receive either a two percent clindamycin phosphate vaginal cream or a placebo for seven days of treatment.

Participants were screened again for BV at one week after treatment and again between 30 to 36 weeks' gestation. Overall, the authors found that nine women in the treatment group (5%) and seven women in the placebo group (4%) had a preterm birth. Again, the authors found that women who screen positive for BV who received treatment had a non-significant increase in their risk of preterm birth compared to women who screened positive and received a placebo (OR: 1.3; 95% CI: 0.5-3.5). [103] In a study by Joesoef et al., a total of 745 women who screened positive for BV, defined as a Nugent score indicative of BV and a pH level greater than 4.5, at 14 to 26 weeks' gestation were randomized to either receive 5gm of 2% clindamycin vaginal cream for one week or a placebo. Overall, no difference was seen in the rate of preterm birth at <37 weeks' gestation between the treatment (15%) and placebo groups (13.5%) (OR: 1.1; 95% CI 0.7-1.7). A non-significant increase in preterm birth at less than 32 weeks' gestation was seen among those who received clindamycin (4.7%) compared to those who received a placebo (2.6%) (OR: 1.8; 95% CI: 0.8-4.2). [104] In a study by Lamont et al., 409 women screened for positive BV or intermediate flora using Nugent's method at less than 22 were randomized to receive either five grams of 2% clindamycin intravaginal cream for three days or a placebo. Women were rescreened 20 to 24 days after initial assessment and given a seven day course of the same treatment if they were positive for BV. Overall, the authors found a significant reduction in the occurrence of preterm birth among women who received clindamycin vaginal cream (4%) compared to the women who received a placebo (10%) (p=0.03). [105] An important component of this study was that nearly all women were treated before 20 weeks' gestation and high percentage (60%) were treated prior to 16 weeks' gestation. Though the authors were unable to show any statistically significant difference in the effect of gestational age at treatment on the outcome, this early treatment time may be the reason why the results from this study

contradict those of most other trials. In a study by Guaschino et al. the authors used a modified version of Spiegel's method to screen women for BV between 14 and 25 weeks' gestation. A total of 112 women who were found to be positive were randomized to receive either intra-vaginal clindamycin 2% cream once a day for seven days or no treatment. Overall, the authors say no difference in the rate of preterm birth between women who screened positive who received clindamycin (12.2%) and women who received no treatment (15.7%) (p=0.78). The authors also saw no difference in the rate of premature rupture of membranes (PROM) (p=0.19) or low birth weight (p=0.32) between the two groups. [106] In a study by Kiss et al. 4155 women were screened for BV using Nugent criteria between 15 and 20 weeks' gestation. For women in the intervention group, the results of this screening were shared with their provider. For women in the control group, both the participant and physician remained blinded to the outcome of the screening. For those in the intervention group who screened positive, treatment consisted of six days of intra-vaginal 2% clindamycin. If a recurrent or persistent infection was discovered, they were treated with 300mg oral clindamycin twice a day for seven days. Overall, 3% of the intervention group and 5.3% of the control group had a preterm birth (p=0.0001). Among women who screened positive for BV, six women in the intervention group and 10 in the control group had a preterm birth (no p-value provided). [107] In a study by Larsson et al. 819 women screening positive for BV by Nugent criteria between 10 and 14 weeks' gestation were randomized to receive either a seven day dose of clindamycin vaginal cream or to remain untreated. There was a non-significant increase in the rate of preterm birth between the intervention group (5.1%) and the control group (6.1%) (OR: 0.84; 95% CI: 0.48-1.47). When the authors looked at spontaneous preterm births and late miscarriages together, there was a non-significant increase in the risk among the control group (3.1%) compared to the clindamycin

group (2.8%) (OR 0.90; 95% CI 0.40-2.02). Interestingly, there was a significant difference in the mean gestation length at delivery between the intervention group (247.6 days) compared to the control group (215.0 days) (p=0.024). [108] In summary, only two of the seven clinical trials conducted using either oral or vaginal clindamycin have found a significant decrease in preterm birth following treatment (Table 2).

Table 2. Randomized controlled trials on clindamycin treatment of BV in pregnancy

Author (Year)	N	Time of BV Diagnosis	Treatment Method	Comparison Group	Odds Ratio (95% confidence interval)
Kurkinen-Raty (2000)	101	12 weeks'	20mg/g clindamycin for 7 days	Placebo	2.1 (0.6-10.0)
Kekki (2001)	375	10-17 weeks'	2% clindamycin vaginal cream for7 days	Placebo	1.3 (0.5-3.5)
Joesoef (1995)	745	14-26 weeks'	2% clindamycin vaginal cream for 7 days	Placebo	1.1 (0.7-1.7)
Lamont (2003)	409	<22 weeks'	2% clindamycin vaginal cream for 3 days + 7 additional days of treatment for persistent infection	Placebo	4% (treatment) vs. 10% (placebo) (p<0.03)[a]
Guaschino (2003)	112	14-25 weeks'	2% clindamycin vaginal cream for 7days	No treatment	12.2% (treatment) vs. 15.7% (control) (p=0.78)[a]
Kiss (2004)	4,155	15-20 weeks'	2% clindamycin vaginal cream for 6 days +300mg oral clindamycin twice daily for 7 days if persistent infection	No treatment [b]	3% (treatment) vs. 5.3% (control) (p<0.0001)[a]
Larsson (2006)	819	10-14 weeks'	2% clindamycin vaginal cream for 7 days	No treatment	Preterm birth: 0.84 (0.48-1.47)

[a] OR and 95% CI not calculated

[b] BV status was not disclosed to physicians, but symptomatic patients may have been treated

Another commonly investigated treatment option is oral metronidazole. In a study among low risk women was performed by Odendaal et al. who examined 150 primigravidae women and 127 multigravidae women who screened positive for BV by Amsel's criteria at less than 26 weeks' gestation. Women in both groups were randomized to receive either 400mg of metronidazole twice a day for two days or 100mg of Vitamin C twice daily for two days. Patients were rescreened for BV four weeks after receiving initial treatment. Those who screened positive were given another course of the same medication as they received the first time. Overall, the authors showed a non-significant increase of preterm birth from 16% among primigravidae women who received Vitamin C to18% among those received metronidazole. Among the multigravidae women, there was a significant increase (p=0.0274) in the rate of preterm birth from 24% of those who received Vitamin C to 43% among those who received metronidazole. [109] In a randomized trial by McDonald et al. the authors randomized women who screened positive for BV and had a heavy growth of *G. vaginalis* at their 18 week prenatal visit a total of 857 women to either 400mg of metronidazole twice daily for two days or a placebo. Women were rescreened at 28 weeks' and those who screened positive were given a second course of their allocated treatment. Overall, the authors showed a non-significant decrease in the risk of preterm birth among those who received metronidazole (4.7%) compared to those receiving a placebo (5.6%) (OR: 0.82; 95% CI: 0.43-1.57). The same non-significant trend was seen whether the authors looked at intention to treat or only at those who actually received the allocated treatment. [110] In a third study done by Carey et al., a total of 1,953 women who had both a Nugent score greater or equal to seven and a vaginal pH level of greater than 4.4 when screened before 23 weeks' gestation. These women were then randomized to either receive either two

doses of 2g metronidazole or a placebo administered before 24 weeks' gestation. A second round of treatment was administered between 24 and 30 weeks' gestation, at least two weeks after the first course. The authors found that the rate of preterm delivery did not differ between the treatment (12.2%) and the control (12.5%) groups (RR 1.0; 95% CI: 0.8-1.2). Similarly, no differences was noted when the authors examined risk of delivery before 35 weeks' (RR: 1.0; 95% CI: 0.7-1.5) and before 32 weeks' (RR: 0.9; 95% CI 0.5-1.5). [111] Hauth et al., randomized 624 women who tested positive for BV by Amsel's criteria at a mean gestational age of 22.9 weeks' gestation to receive either a placebo or a combination of 250mg of metronidazole three times a day for seven days plus 333mg erythromycin three times a day for 14 days. Among those receiving treatment, 26% delivered a preterm infant compared to 36% of the placebo group (OR: 1.4; 95% CI 1.1-1.8). [112] Finally, a study by Morales et al. randomized 80 women with a history of preterm birth who screened positive for BV at 13 to 20 weeks' gestation by Amsel's criteria to either a placebo or 250mg of oral metronidazole three times a day for seven days. Overall, the investigators saw a significantly lower rate of preterm birth among those in the treatment group (18%) versus those in the control group (37%). [113] In summary, studies of metronidazole as treatment for BV during pregnancy have largely shown non-significant results. Some of the information seems to indicate that women receiving treatment may even be at an increased risk of preterm birth (Table 3).

Table 3. Randomized controlled trials on metronidazole treatment of BV in pregnancy

Author (Year)	N	Time of BV Diagnosis	Treatment Method	Comparison Group	OR (95% CI)
Odendaal (2002)	277	<26 weeks'	400mg metronidazole 2x/day for 2 days + 2 additional days for persistent infection	100mg Vitamin C twice daily for two days	Primigravidae: 18% (treatment) vs. 16% (control) (NS)[a] Multigravidae: 43% (treatment) vs. 24% (control) (p=0.0274)[b]
McDonald (1997)	857	18 weeks'	400mg oral metronidazole 2x/day for 2 days + repeat treatment for persistent infection	Placebo	0.82 (0.43-1.57)
Carey (2000)	1953	<23 weeks'	Two doses 2g vaginal metronidazole + repeat treatment two weeks later	Placebo	1.0 (0.8-1.2)
Hauth (1995)	624	22.9 weeks' [a]	250 mg oral metronidazole 3x/day for 7 days + 333mg erythromycin 3x/day for 14 days	Placebo	1.14(1.1-1.8)
Morales (1994)	80	13-20 weeks'	250mg oral metronidazole 3x/day for 7 days	Placebo	18% (treatment) vs. 37% (control)[b, d]

[a] No p-value provided, not significant
[b] Odds ratio and 95% CI not calculated
[c] Mean gestational age at enrollment
[d] No p-value provided, significant

While most of the studies (n=13) done have not been able to demonstrate any improvement in preterm birth rates with clindamycin or metronidazole treatment, a small number (n=4) have shown a protective effect. Those that have shown lower rates have mainly been done among women who were known to be at a higher risk due to previous preterm births. For this reason it is not recommended that pregnant women be routinely screened for BV during pregnancy, as treatment for asymptomatic individuals does not appear to reduce the risk of adverse outcomes and may actually increase a woman's odds of delivering early. In women with BV who have had previous preterm births, clinicians may use their discretion in providing treatment. [114]

2.1.3 Epidemiology

Using data from the 2001-2002 and 2003-2004 National Health and Nutrition Examination Survey (NHANES), studies have been able to look at prevalence of BV among women in the United States. For this study, BV was diagnosed in a research lab using Nugent's criteria and demographic information was obtained through self-report on questionnaires. Overall, the prevalence of BV was nearly 30% for all women ages 14-49. [32] This number represents roughly 21.7 million women in US with BV. [35] Investigators looked at possible differences in rates among various subgroups. No difference was seen across the age groups included in this study or across the various income levels. Significant differences were found for race and education level. Overall, non-Hispanic blacks had the highest rate (51.6%), followed by Mexican Americans (32.1%) and non-Hispanic whites (23.3%). Other significant differences were found with education, where those with a high school education or higher were less likely to be positive (26%) compared to those with less education (33-34%). [32] When a logistic regression model

was used to adjust for socio-demographic information, the increased risk of BV among Mexican American women became non-significant; however, the increased risk among non-Hispanic blacks remained strong (OR: 3.13; 95% CI: 2.58-3.80). [32] Information from this data also indicates that 84% of women diagnosed with BV reported no symptoms. [35]

A number of studies have reported similar racial disparity in BV. [49, 51, 115, 116] This difference is best demonstrated by two large US studies. The ABC study conducted in Seattle, Washington, enrolled a population-based sample of 400 parous women in a longitudinal study. At baseline, the investigators found a highly significant difference in the prevalence of BV by Nugent's criteria among white (17%) and African American (45%) pregnant women ($p<0.0001$). [50] The second enrolled 1,886 pregnant women from obstetric practices at the Hospital of the University of Pennsylvania and found that 14% of the non-African American women enrolled had BV by Nugent's criteria compared to 46% of pregnant African American women. [52] A portion of the difference in these rates can be explained by other known risk factors, including socioeconomic status, douching, and sexual behavior. Still, studies which adjust for these factors continue to report large difference in the prevalence of BV between racial groups. A cohort study of 1,135 women from across the US, including 900 blacks, investigated a number of characteristics that might explain these differences. After adjusting for all important and significant socio-demographic and lifestyle factors, black women remained twice as likely as white women to have BV or intermediate flora as determined by Nugent's criteria. [117] This study indicates that other factors are at play in causing these increased rates. The same study associated black race with lack of H_2O_2-producing lactobacilli, which would predispose these women to developing BV. [117] While no conclusive answer exists for the different rates, a number of theories exist. One popular theory is that black women have higher chronic stress

levels throughout life, which may influence their vaginal ecosystem. [118] A second possible explanation is that blacks have a more alkaline vaginal pH compared to whites, increasing their susceptibility to an overgrowth of abnormal bacteria. [117] More research is needed to determine the risk factors that may lead to differences in prevalence rates among racial and ethnic groups, both in the United States and around the world.

2.1.3.1 Prevalence in India

In India, few studies have estimated the prevalence of BV. Most studies have centered around the northern city of New Delhi. In a study at the Regional STD Centre at Vardhaman Mahavir Medical College (VMMC) and Safdarjung Hospital in New Delhi, information on reproductive infections was collected on 78,617 patients over a period of 14 years, beginning in January 1990. Most patients (~80%) seen were from the urban area of New Delhi, with very few coming from rural underserved areas. Only 3,966 of those patients were female. Information was divided into four time periods, each spanning roughly three years (1990-1993, 1994-1997, 1998-2001, 2002-2004). From this data, it appears the prevalence of BV steadily decreased from the first time period, where 13.5% of females seen were diagnosed with BV, to the last time frame, where only 4.5% of females seen were diagnosed with BV. [119] It is unclear from the information provided how patients were screened for BV and whether this method remained consistent throughout the study time frame. It is likely that the presented data is an underestimation of the true rate. This may also be due to the decline in the number of attendees and cases of all STIs that were reported during these years. The number of data reported from females declined dramatically throughout the study period, with the initial years reporting visits from 1,733 women and the last period only reporting data for 622. Since women had to be referred either through their husbands or the gynecology department, many cases of BV and other infections may have been dealt with

by physicians outside of the clinic. [119] Though the paper makes no reference to these issues, there is the possibility that patients began seeking treatment at other facilities that became available during these years. A cross-sectional study of 300 women from antenatal and gynecological clinics in New Delhi found that 14.3% of women had BV by Amsel's criteria.[120] By contrast, a community cross-sectional study enrolling 301 women from an urban slum outside New Delhi found that the prevalence of BV was 41.5% by Amsel's or Nugent's criteria, with 40.2% of symptomatic women and 45.7% of asymptomatic women receiving a diagnosis.[121] One study in India looked only at 502 asymptomatic pregnant women at 14-28 weeks' gestation in a rural area near New Delhi. Using Nugent's criteria, the prevalence of BV was 8.6%, compared to 6.2% using Amsel's criteria. [122] A population-based study of various housing areas in New Delhi looked at 122 women from an urban slum, 60 from a middle class area and 55 from the rural area (n=237). Using Nugent's criteria, they found that 32.8% of the sample had BV. [123] The prevalence of BV varies greatly around the city of New Delhi depending on the population sampled and the diagnostic tests used (Table 4). Further studies will be needed to investigate the possible risk factors responsible for the differences.

Table 4. Studies of BV prevalence in and around New Delhi, India

Author (Year)	Study Design	N	Method of BV Diagnosis	Population	Prevalence of BV
Ray (2006)	Longitudinal	3,966	N/A*	STD clinic, New Delhi	4.5-13.5%
Sharma (2004)	Cross-sectional	300	Amsel	Antenatal and gynecology clinics, New Delhi	14.3%
Sodhani (2005)	Cross-sectional	301	Amsel and Nugent	Urban slum, New Delhi	41.5%
Dadhwal (2010)	Cross-sectional	502	Nugent and Amsel	Rural New Delhi	8.6% (Nugent) 6.2% (Amsel)
Bhalla (2007)	Cross-sectional	237	Nugent	Community based, New Delhi	32.8%

*Method of diagnosis not reported

A few studies have looked at other geographic regions of India and found similar prevalence estimates. The largest study was conducted in Goa and recruited 2,494 women ages 18-50 from the community. Using Nugent's criteria, this study found an overall prevalence of 17.8%. [124] Similar results were found in four cross-sectional studies from other areas. The first was a study of 582 female sex workers in Chennai, where the overall prevalence by Nugent's criteria was found to be 14.1%. [125] The second studied 898 sexually active women 15-30 years of age from reproductive health care clinics in Mysore and found prevalence rates by Nugent's criteria were found to be 19.1% (95% CI: 16.2-22.2). [126] The third conducted a cross-sectional study among female sex workers in Surat and found a prevalence of 17.4% by Nugent's criteria. [127] The fourth looked at 53 women presenting with abnormal vaginal discharge to the outpatient department at a hospital in Kolkata. The investigators found that 24%

of the women had BV by Nugent's criteria. [128] A cross-sectional study looking at a tribal population found a much higher rate of BV than reported in any other publication based on studies done in India. This analysis looked at 17 tribal villages in Madhya Pradesh looked at 326 individuals with STI symptoms, including 211 women. Using clue cells as the main method of diagnosis, 64.1% (95% CI: 56.5-71.0) of women were diagnosed with BV. [129] The high prevalence in this study can be attributed to the fact that only individuals with symptoms of one sexually transmitted or reproductive tract infection were included in the population. In addition, the investigators used the presence of clue cells as the diagnostic criteria for BV. Though other Indian studies have shown the presence of clue cells to have a high sensitivity (67-77%) and specificity (92-94%) compared to Amsel's criteria for the diagnosis of BV [121, 128], use of the full set of Amsel's criteria or Nugent's criteria is preferable.

In summary, BV prevalence rates in India range from 5-64%. [119, 129] As studies are sparse, more research is needed to determine the prevalence in various regions throughout the country using standardized techniques for BV assessment. From information available, it appears that geographic [121, 124, 125], ethnic [129], and socioeconomic [119, 125] status may play a role in determining prevalence. However, as the evidence for this is weak, additional studies examining a range of risk factors for BV among women in India are needed (Table 5).

Table 5. Studies of BV prevalence in India (excluding New Delhi area)

Author (Year)	Study Design	N	Method of BV Diagnosis	Population	Prevalence of BV
Patel (2006)	Cross-sectional	2,494	Nugent	Goa	17.8%
Uma (2005)	Cross-sectional	582	Nugent	Sex workers, Chennai	14.1%
Madhivanan (2008)	Cross-sectional	898	Nugent	Reproductive health clinics, Mysore	19.1%
Rao (2009)	Cross-sectional	211	Clue cells	Tribal villages, Madhya Pradesh	64.1%
Shethwala (2009)	Cross-sectional	300	Nugent	Sex workers, Surat	13.33%
Modak (2011)	Cross-sectional	53	Nugent	Hospital outpatient clinic, Kolkata	24.0%

2.1.4 Risk Factors for BV

BV does not have one single cause. Though sexual practices seem to play a large role in the development of infection [29, 130-134], there are a number of other risk factors that seem to be important. Douching [42-44, 135-138] and use of contraceptives [132, 139-146] are two of the most researched and developed areas of research and have the most convincing evidence regarding exposure. Hygiene is a potential risk factor in the development of BV. [147-149] However, current research is lacking and needs to be further developed before any conclusions can be drawn. A number of other risk factors have also been investigated and found to be potentially important, including smoking[45, 150] and stress levels.[48, 50, 151]

2.1.4.1 Douching

Current research indicates that there are no known health benefits to douching. [136, 137] A number of studies have shown a link between douching and development of BV. A retrospective study of 947 women with BV looked at the number and type of lactobacilli identified in vaginal flora and analyzed the results based on risk factors assessed in interview. A total of 756 women did not have H_2O_2-producing lactobacilli present at the time of analysis. Among women with BV by Nugent score, the odds of not having H_2O_2-producing lactobacilli were 2.6 (95% CI: 1.2-5.5) times higher among those who douched in the past week and 2.7 (95% CI: 1.1-6.4) times higher for those who reported douching at least twice in the past month. After adjusting for other significant factors, this relationship remained significant (OR_{adj}: 2.5; 95% CI: 1.1-6.0). [152] Since H_2O_2-producing lactobacilli may play a major role in the development of BV, this information may provide insight into the reason why someone relapse while others are cured following treatment. A cross-sectional study of 496 women assessed for BV by Nugent score self-reported risk factors and other socio-demographic information. Women who reported use of a vaginal douche in the past two months had 3.6 times (95%CI: 2.0-6.2) the risk of BV than those women who reported not douching or douching less frequently. This relationship weakened, but remained significant when adjusted for ethnicity, education, and hormone use (OR_{adj}: 2.9; 95% CI: 1.5-5.6). [131]

Several other studies have been unable to find a relationship between douching and BV. A cross-sectional study conducted among women ages 16 to 35 who reported having sex with other women found no relationship between douching in the prior 30 days and BV (RR: 1.53; 95% CI: 0.90-2.58). [31] Another cross-sectional study looking at women $\leq$ 12 weeks' gestation found a significant increase in the odds of BV among women who reported douching during

pregnancy (OR: 1.80; 95% CI: 1.31-2.46), but this became non-significant when adjusted for age, race, socio-demographic information, smoking, and STD history (OR: 1.20; 95% CI 0.86-1.57).[52] A cross-sectional study of sex workers in Brazil found no significant relationship between douching and development of either grade II or grade III vaginal flora, even when breaking out douching habits by reason and frequency (adjusted Prevalence Risk: 1.17; 95% CI: 0.80-1.71).[44] Finally, one study combined both cross-sectional and prospective analysis to analyze multiple time-points for 1193 women who were followed for 3 years, with douching assessed every six months. In the cross-sectional analysis, women who douched during the period analyzed were only at an increased risk for BV if they also had BV at the prior visit. When the data was analyzed longitudinally, no overall association was found for douching and BV, but among women with intermediate flora, there was a slight increase in the risk of acquiring BV (HR: 1.5; 95% CI: 1.1-2.4).[42] These data suggest that douching may only be a risk factor for certain categories of women who also have other strong risk factors for the development of BV.

The majority of studies done to look at the association between douching and BV are cross-sectional in nature. As many women douche as a way of dealing with the symptoms of BV determining a temporal relation is difficult. Two studies have been able to overcome some of these difficulties to better understand the relationship. First, a longitudinal study of 39 women who douched allowed women to continue douching normally for the first four weeks, and then asked them to stop for a follow-up period of 12 weeks. Finally, participants were allowed to either continue douching cessation or return to their normal practice for the last four weeks. Vaginal samples were taken twice weekly during the first two stages and once at the end of the last phase. Overall, there was not a significant reduction in BV during the douching cessation

phase (ORa: 0.76; 95% CI 0.33-1.76). When only women who reported douching for the purpose of removing menstrual blood were analyzed, a significant reduction was seen (ORa: 0.23; 95% CI 0.12-0.44).[135] This same difference was not seen when looking at women who reported douching to remove vaginal odor or to feel clean. While the author postulated that there might be some synergistic effect between disruption in vaginal flora due to menstruation and douching, it may also be possible that the effect is seen only among women who were not douching as a way to deal with symptoms of abnormal vaginal flora. A second longitudinal study followed 3,620 non-pregnant women for a period of one year. Participants were assessed quarterly for BV by Nugent's criteria and asked about douching practices in the prior three months. The investigators used marginal structural models to adjust for douching practices, including adjustment for douching practiced by women who already had BV. Overall, they found that women who practiced douching were at a 21% increased risk of developing BV (OR: 1.21; 95% CI: 1.08-1.38).[43] The evidence from these two studies suggests that for women who are not douching as part of self-treatment for vaginal symptoms, douching increases the risk of developing BV. This information may explain why evidence from cross-sectional studies is mixed on the overall risk and effect of vaginal cleansing.

Evidence for douching as a risk factor for BV is still mixed. While much evidence points toward a moderate association, an equal amount points to no relationship. Likely, douching is one of many risk factors that lead to infection in individuals who are already at a higher risk. As a modifiable risk factor, douching is something that can be discouraged by medical professionals as a way to help avert new and recurrent BV.

2.1.4.2 Sexual risk factors

Though BV is often included in references relating to sexually transmitted infections (STIs), it is not considered to be part of this category. While there are sexual risk factors for contracting BV and some transmission may occur via intercourse, not all infections occur this way. As BV is a polymicrobial infection, it is possible that this difference may be due to certain bacteria being sexually transmitted infections while others are transmitted via other routes. There are a number of sexual risk factors that have been shown to be possibly related to BV infection.

Hormonal contraceptive use has been shown to have a protective effect against BV infection in a number of studies. A cohort study of 330 women from two STD clinics in Baltimore was studied to look at the effect of hormonal contraception on BV diagnosis. Compared to women who were not using any contraceptives, those using a progestin only method had a decreased risk for subsequent BV diagnosis (OR_{adj}: 0.42; 95% CI: 0.20-0.88). Women using a combination method had a decreased, but non-significant risk of BV (OR_{adj}: 0.66; 0.39-1.10).[153] In one of the largest cohort studies to date, 3077 women were followed to look at the association between use of various contraceptives and BV. A decreased risk of BV prevalence among pill users (OR: 0.76; 95% CI: 0.63-0.90) and injection/implant users (OR: 0.64; 95% CI: 0.53-0.76) was noted. [140] In a comparative cohort study of 123 IUD users and 108 oral contraceptive users, the authors found that IUD users had nearly three times the risk of developing BV compared to those using oral contraceptives (RR:2.8; 95% CI: 1.5-5.1).[154] Results from these and other studies have almost universally found a decreased risk of BV among hormonal contraceptive users. [139, 141, 142, 155, 156]

Two theories exist as to why hormonal contraceptives may decrease the risk of BV. First, adequate estrogen levels increase glycogen production, which serves as a food source for

Lactobacilli. Second, hormones, especially progestin, inhibit uterine bleeding. As menstruation causes shifts in the vaginal flora, this inhibition may help to maintain overall balance in the vagina.[157]

As the previously discussed study indicates[154], many studies show that intrauterine device (IUD) users are at an increased risk of developing BV.[139, 141, 144, 145, 154, 158] Many of the problems associated with IUDs are a result of an early version, the Dalkon Shield, which had a multifilament string which allowed easy passage for bacteria from the vagina to the uterus. The Dalkon Shield was associated with a high rate of infection and was removed from the market in the mid-1980s as a result. Current IUDs use a monofilament string and are considered relatively safe for use. Current research indicates that IUD use is not associated with increased risk of BV. A 2008 study compared the change in vaginal flora following insertion of a copper IUD in 78 women compared with a progesterone-incorporated IUD (Mirena) inserted in 94 women. Patients were assessed for BV at a visit less than a month before insertion, again at four to six weeks post-insertion, and a third time at 6 months post-insertion. At the first follow-up appointment, 3.9% of those receiving a copper IUD and 1.4% of those receiving Mirena who had normal flora at insertion had developed BV using Ison-Hay criteria ($p=0.38$). At the six month follow-up, 7.3% of those using the copper IUD and 2.8% of those with Mirena who had normal flora at baseline had developed BV (p-0.30).[159] Interestingly, this study did show a significant difference in the patient reported rates of abnormal vaginal discharge among those receiving Mirena compared to those receiving a copper IUD ($p=0.04$), which is likely due to other changes in the uterine lining associated with hormonal IUD use. [159] Another longitudinal study from 2011 examined changes in vaginal flora of 286 women for up to two years post-insertion of a hormonal IUD (Mirena) found that there was no significant difference in the rate of infection a

year after insertion (no p-value provided), though they did show a slight increase in risk among first time users for all infections (OR: 1.7; 95% CI: 1.1-2.8). However, this last number included BV, *Candida*, and aerobic vagintis, making it difficult to determine whether there was a true increase in the rates of BV. [160] Other studies have shown that rates of BV are higher among IUD uses than among those using oral contraceptives. [140, 161] As previously discussed, oral contraceptives may have a protective effect. Those with IUDs may not be at an increased risk, but have a normal risk that appears high when compared to oral contraceptive users. This may be especially true for studies involving copper IUDs, which are commonly used outside of the United States. IUDs containing similar hormones to oral contraceptives may have a similar protective effect. Overall, any increased risk associated with current IUDs is small and may be due to other risk factors for women choosing to use IUDs over other forms of contraceptives.

Condoms also seem to lower the risk of BV infection. A study of 871 high risk women in a case-crossover analysis was followed for three years. Those who reported consistent condom use were half as likely to develop BV compared to those who did not use condoms (OR: 0.55; 95% CI: 0.35-0.88). When the authors compared those with normal flora to those with BV by Nugent criteria, excluding the intermediate flora category, they found an even stronger relationship (OR: 0.37; 95% CI: 0.20-0.70).[132] Additional studies have found a similar reduction in risk for those using condoms, with the greatest benefit coming from consistent use. [134, 139, 142] Still, some studies have found null results. [143, 162-164] The evidence from studies of condom use and BV provide insight into one of the potential pathways of transmission. Sexual activity is a consistently cited risk factor for BV throughout the literature, with commonly found factors including number of sexual partners[130, 133] and new sexual partners.[130, 165-168] Perhaps the most convincing evidence comes from lesbian studies, where concordance

between partners is typically found to be high. [31, 169, 170] Conversely, many patients who develop BV report not being sexually active and others do not have any of the high risk behaviors.[171] Overall, evidence points to multi-causal pathways, with sexual activity and behavior being a strong exposure.

2.1.4.3 Hygiene

The association between rectal bacteria and the development of BV is a newly developing area of research. In a study of 148 women with BV by Amsel's criteria and 69 women with healthy vaginal flora, rectal samples were taken and examined for four different organisms associated with BV. In women with BV, *M. mulieris* was found in 56%, *M. cu*rtisii in 62%, *G. vaginalis* in 45%, and *M. hominis* in 54%. These percentages are much higher than among the healthy women, where the most commonly found pathogen, *M. curtisii*, was only found in 14% of samples.[147] A more recent study looking at 132 pregnant women examined at 35-37 weeks' gestation found a number of similarities between bacteria colonies in the vagina and the rectum. A total of 63 species were examined for this study. Nine were found only in vaginal colonies, 26 only in rectal colonies, and 29 in both locations.[148] The findings from this study are mainly applicable to species of lactobacilli, as are the results from many other studies. Specifically, a number of studies point to *L. crispatus*, *L. gasseri*, and *L. jensenii* as being harbored in both the vagina and rectum. [148, 149, 172] There is less evidence that BV-associated bacteria are also housed in the rectum. One major study found that there was little similarity between the Bifodobacterium species found perianally in women with the bacteria found at vaginal sites, with the exception of *G. vaginalis.* [173] Given this information, there is a growing body of literature pointing toward the role of rectal colonies in the prevention and development of BV. If a link does exist, hygiene and sanitation may be potentially modifiable risk factors for BV.

2.1.5 Adverse outcomes associated with BV among pregnant women

BV has been associated with a number of adverse pregnancy outcomes, including spontaneous abortion (loss of a pregnancy at <22 weeks' gestation), and birth of a preterm (<37 weeks' gestation), low birth weight (<2,500 grams), small for gestational age (<10^{th} percentile by sex and gestational age) and growth restricted infant (<5^{th} percentile by sex and gestational age).

2.1.5.1 Spontaneous abortion

The link between BV and spontaneous abortion remains unclear. While many studies have found an association between the two, other studies have failed to find an increased risk of spontaneous abortion in women with BV or have only shown an association at specific time points. The majority of studies have been prospective cohorts that recruited women from prenatal clinics during the first trimester. In an early cohort study of 461 British women who presented to a hospital for their first antenatal clinic between nine and 16 weeks' gestation found an association between grade II and grade III flora, as determined using a modified version of Spiegel's method, and spontaneous abortion and preterm birth (OR_a: 5.5; 2.3-13.3).[70] As this study did not separate the two outcomes for analysis, it is difficult to determine whether the large odds ratio is a result of an increase in the risk of spontaneous abortion, preterm birth, or both. In two cohorts of women being followed to determine the best method of treatment for a variety of vaginal infections, a total of 1138 women were screened for BV at registration (mean 16-18 weeks' and 20 weeks' gestation) using Amsel's criteria. Overall, the researchers found that women with BV had a three-fold increased risk for spontaneous abortion. (RR: 3.1; 95% CI: 1.4-6.9).[20] Another cohort study using Amsel's criteria to diagnose 228 Belgian women at <14

weeks' gestation found that women with BV were 5.4 times more likely to have a spontaneous abortion than those without BV (RR 5.4 95% CI: 2.5-11.0) In addition, women with a grade III lactobacillary flora as defined by Schroder's classification system (RR: 5.4; 95% CI: 2.0-7.8) and women with clue cells (RR, 5.4: 95% CI, 2.5-11.0) were also at an increased risk of spontaneous abortion compared to women with normal slides.[174] Tripathi et al. enrolled 200 women at their first prenatal visit (<18 weeks' gestation) at a tertiary hospital in New Delhi, India, and tested them for BV using Amsel's criteria. Overall, the investigators found that women with BV were 7.5 times more likely to have a second trimester abortion compared to women without BV (OR 7.50; 95% CI: 1.28-56.0).[175] While this study found an extremely high risk, only eight spontaneous abortions were identified within the study population, giving little data with which to calculate risk. The authors did not provide a mean gestational age at enrollment, but based on the fact that new data for first trimester abortions were reported, it is likely the majority of women was recruited in the second trimester and was past the periods of highest risk. In a prospective study of Italian women seen in an antenatal clinic at $\leq$ 10 weeks' gestation, Guerra et al reported that women who'd experienced at least one preterm birth who screened positive for BV using Nugent's criteria between 3 and 12 weeks' had nearly a six fold increased risk of spontaneous abortion compared to women with normal flora after adjusting for previous miscarriages and prior preterm births (ORa: 5.71; 95% CI: 2.92-11.1).[176] In addition, they showed that women with intermediate flora had a similar increase in risk (ORa: 5.30; 95% CI: 2.92-9.60).[176] The most convincing evidence for the link between BV and spontaneous abortion comes from two meta-analyses performed by Leitich et al. The first, conducted in 2003, looked at three studies with a total of 856 participants and found almost a ten-fold increase in the risk of spontaneous abortion among women with BV (OR: 9.91; 95% CI: 1.99-49.34). [177] In

2007, they updated the analysis and looked at five papers examining the relationship between late miscarriages and found that women with BV were at a significantly increased risk of spontaneous abortion (OR 6.32; 95% CI: 3.65-10.94) and women with intermediate flora had a lower, non-significant increase in risk (OR 2.7; 95% CI: 0.94-8.14).[178]

Other studies have shown no association between BV and spontaneous abortion. In a cohort study of 168 South African women recruited at <30 weeks' gestation, Govender et al. found no significant difference in the rate of spontaneous abortion between women with BV diagnosed using Nugent criteria, women with other vaginal infections, and women with no infection.[179] However, the high rate of infection (71%), in particular BV (52%), made comparison difficult due to the small number of women who were in the normal category. Second, the average gestation age at enrollment was 26 weeks', meaning that a large number of women in the study were already past the cutoff for spontaneous abortion before they began observation. In a large cohort study of 1916 participants screened for BV using Nugent criteria at ≤12 weeks' gestation, Nelson et al. found no relationship between BV and spontaneous abortion (HR: 1.17; 95% CI: 0.78-1.75). This relationship remained the same when the authors adjusted for gestational age at enrollment, maternal age at enrollment, cigarette use, African-American race, vaginal bleeding, and a history of incompetent cervix (HRa: 0.84; 95% CI: 0.38-1.87). A significant result was found when continuous scores were used instead of a dichotomous exposure (HRa: 1.24; 95% CI: 1.02-1.64). In addition, when the authors compared women with scores of seven to 10 (BV) with women with scores of zero to three (normal), they found a 2.5 fold increase in risk for spontaneous abortion among those with higher scores (HRa: 2.49; 95% CI: 1.13-5.48).[180] These results may indicate that a larger change in the vaginal flora is associated with an increased risk of spontaneous abortion.

Some studies have shown no overall association between BV and spontaneous abortion, but have demonstrated an increased risk for late miscarriage. Llahi-Camp et al. performed a case-control study of 500 non-pregnant women who had had at least three consecutive miscarriages to look at whether BV diagnosed using Spiegel's method was associated with early (≤13 weeks' gestation) and late (>13 weeks' gestation) miscarriage. They found that women who had experienced at least one late miscarriage were more likely to have BV (27/130; 21%) compared to women who had only experienced early miscarriage (31/370; 8%) ($p<0.001$). This same association held when they only looked at women who'd had at least one term pregnancy ($p<0.001$).[181] In a larger cohort study of 1201 British women recruited at <10 weeks' gestation, Oakeshott et al. found no relation between BV diagnosed using Nugent's method and miscarriage at <16 weeks gestation (OR 1.15; 95% CI: 0.70-1.87). However, when the investigators looked at spontaneous abortion in three different time categories, they found no association for loss at <10 weeks' gestation (OR 0.53; 95% CI 1.19-1.47) or at 10 to 12 weeks' gestation (OR 1.32; 95% CI 0.67-2.62), but found a positive association between BV diagnosis and spontaneous abortion at 13 to 15 weeks' gestation (OR 3.45; 95% CI: 1.16-10.29).[182] However, the smallest number of spontaneous abortion occurred during this last time category (14) compared to the earlier time categories (51 and 56, respectively). This may contribute to increase odds ratio and wide confidence interval. While the study recruited women at <10 weeks' gestation, seven weeks' was the mean gestational age at enrollment. Further, this study only followed women until 16 weeks' gestation, providing a narrow window. Finally, women were interviewed about their pregnancy outcome at 16 weeks'. Only a very small amount (9%) of the data came from medical charts. Women may fail to report spontaneous abortion or be unaware of them at the time of interview, contributing to the low number. In a follow-up to this study of 912

pregnant women, Oakeshott et al. looked at the same cohort, this time looking for an association between late miscarriage (13-23 weeks' gestation) and BV. Overall, they found BV- positive women were four times as likely (RR: 4.0; 95% CI: 1.3-12.1) as BV-negative women to have a spontaneous abortion at this later time point.[183] This result is consistent with the earlier study where they showed a relationship between the latest time point measured (13 to 15 weeks') and BV. The above studies have a number of important limitations. First, they only enrolled women who presented to a prenatal clinic, and, thus, only included women with clinically recognized pregnancies. Second, women were only tested for BV at enrollment. Studies have shown that vaginal flora shifts can occur very quickly. These studies are unable to identify whether the woman had an infection at the time of the spontaneous abortion. Third, only two of the studies adjusted for confounders. [176, 180] Previous miscarriages, as well as having carried a previous pregnancy to term, were adjusted for in one [176], while the other adjusted for maternal age, race, cigarette use, and vaginal bleeding. [180] All of these factors play a potential role in spontaneous abortion and may explain some of the difference in findings between studies. Finally, most of these studies enrolled a small sample size [70, 174-176, 181] and thus have wide confidence intervals (Table 6).

Table 6. Select prospective cohort studies of spontaneous abortion and BV

Author (Year)	Study Design	N	Method of BV Diagnosis	Time of BV Diagnosis	Results (95% CI)
Donders (2000)	Prospective cohort	218	Schroder	<14 weeks' gestation	RR: 5.4 (2.5-11.0)
Guerra (2006)	Prospective cohort	242	Nugent	≤9 +6 weeks' gestation	OR_a: 5.71 (2.92-11.1)
Hay (1994)	Prospective cohort	461	Modified Spiegel	<16 weeks' gestation	OR_a:5.5 (2.3-13.3)
McGregor (1995)	Prospective cohort	1138	Amsel	16-20 weeks' gestation	RR: 3.1 (1.4-6.9)
Nelson (2007)	Prospective cohort	1916	Nugent	<12 weeks' gestation	HRa: 0.84 (0.38-1.87)
Oakeshott (2002)	Prospective cohort	1201	Nugent	<10 weeks' gestation	RR: 1.14 (0.70-1.87)
Oakeshott (2004)	Prospective cohort	974	Nugent	<10 weeks' gestation	RR: 4.0 (1.3-12.1)[2]
Tripathi (2003)	Prospective cohort	155	Amsel	<18 weeks' gestation	OR: 7.50 (1.28-56.0)

[1]Mean age at gestation for entry to study
[2]RR is for late miscarriages (13-23 weeks' gestation) only

To overcome the bias that occurs by only recruiting women with a clinically recognized pregnancy, some studies have recruited women undergoing in-vitro fertilization (IVF) treatment. In these instances, the investigators are able to determine BV status prior to conception, determine the exact date that conception occurred, and closely monitor women for early pregnancy losses. A British cohort study of 301 women attending an IVF treatment found that BV diagnosis using a modified version of Spiegel's method was not associated with increased risk of spontaneous abortion (no p-value provided).[184] In a cohort study of 771 women undergoing IVF at a hospital clinic in England, Ralph et al. found that women diagnosed with BV using a modified version of Spiegel's method were twice as likely to have a spontaneous abortion as those without BV (RRa 2.03; 95% CI 1.09-3.78). Additionally, this study divided

spontaneous abortions into four categories based on the timing. Notably, women with BV were 2.5 times more likely to have a preclinical pregnancy loss, defined as a positive pregnancy test followed by spontaneous abortion before 6 weeks' of gestation and before confirmation of the pregnancy by ultrasonography, than those without BV (RRa: 2.69; 1.47-4.92).[185] In a cohort study of 91 women presenting for their first IVF cycle at the University of Washington, there was no significant association between diagnosis of BV by Nugent's criteria prior to embryo transfer and subsequent pregnancy loss five weeks later when the authors compared the women with intermediate flora to those with normal flora (p=0.2). A comparison between women with BV and those with normal flora was not undertaken because only three women with BV became pregnant following the first round of IVF treatment, compared to 12 with intermediate flora and 26 with normal flora, providing little statistical power to test the association. [186] While these studies are able to capture data from conception onward, the results are not generalizable. Women in these studies suffered from an array of reproductive problems including endometriosis[184], ovulatory disorder[184], recurrent miscarriage[185], polycystic ovary syndrome[185], and varying causes of infertility more often than would be expected in the general population.

If an association between spontaneous abortion and BV exists, it is unknown exactly what the biological pathway would be. Since BV is associated with endometritis, it is a potential mediator between BV and spontaneous abortion. [187, 188] On the other hand, ascent of bacteria from the vagina through the cervix during pregnancy may cause deciduitis, chorioamnionitis, and amniotic fluid infection, all of which may play a role in spontaneous abortion.[187, 189]

2.1.5.2 Preterm Birth

The literature surrounding the association between BV and preterm birth is also conflicted. Overall, the literature suggests that the risk for preterm birth may be greatest in women who have abnormal flora early in pregnancy. Four prospective cohort studies screening women for BV at <22 weeks gestation have found that women positive for BV by gram stain have an increased risk of preterm birth, with significant ORs ranging from 1.1-6.9. [175, 176, 190, 191] The first of these studies screened 490 pregnant women in Indonesia for BV by gram stain at 16 to 20 weeks' gestation and again at 28 to 30 weeks' gestation. They found significant results when screening occurred at<20 weeks gestation (OR: 2.0, 95% CI: 1.0-3.9), but not when screening occurred at a later time point (OR: 1.5, 95% CI: 0.7-3.0).[192] Results are mixed regarding the association between the time of screening for BV and preterm birth. Two prospective studies screened women during the second trimester, the first between 23 and 26 weeks' gestation. This study found that BV diagnosed as a vaginal pH >4.5 and a gram stain score ≥7 was associated with an increased risk of preterm birth (OR: 1.4, 95% CI: 1.1-1.8).[193] A second study diagnosed 635 pregnant women by gram stain at <35 weeks' gestation and found an increased risk of preterm birth (RR:3.1, 95% CI: 1.8-5.4).[88] In a meta-analysis of 20,232 pregnant women, BV was associated a 2-fold risk for preterm delivery at <37 weeks (OR: 2.19, 95% CI: 1.54-3.12).[177] A prospective study of 1,026 women screened for BV using a modified Spiegel method at the first prenatal visit found an increased risk for preterm birth among women with BV (OR: 2.4; 95% CI: 1.1-4.7) and a similar risk for those with abnormal flora, but not BV (OR: 2.4; 95% CI: 1.2-4.8). [194] Some studies have reported that diagnosis of BV in the first or second trimester is more predictive of preterm birth, with RRs ranging from 2.0 to 3.3. [176, 178, 192, 195] One prospective cohort study of 490 women screened for BV found that women screened at 16-20

weeks' gestation had a significantly increased risk of preterm birth (RR: 2.0; 95% CI: 1.0-3.9), but women screened at 28-32 weeks' gestation did not have a significantly increased risk (RR: 1.5; 95% CI: 0.7-3.0).[192] In a meta-analysis of 20,232 pregnant women, BV was associated with a 2-fold increased risk for preterm delivery at <37 weeks' (OR: 2.19; 95% CI: 1.54-3.12). The meta-analysis included both high and low risk women screened between 9 and 30 weeks' gestation, with differing criteria for BV diagnosis.[177] A subgroup of individuals from this analysis who were screened at <16 weeks of gestation had a higher risk for preterm delivery than those screened at <20 weeks with odds ratios of 7.55 (95% CI: 1.80-31.65) and 4.2 (95% CI: 2.11-8.39), respectively.[177] This meta-analysis was later refined to include literature published after May 2005, adding 14 studies and 10,286 patients to the previous analysis resulting in a total of 32 studies and 30,518 patients.[178] This analysis found a similar increase in risk for preterm birth among women with BV as what was reported in the earlier analysis (OR: 2.16, 95% CI: 1.56-3.00). When additional analyses were done to determine if the risk for preterm birth was different depending on when screening was performed, no significant differences were found(OR not reported).[178] However, results are mixed as others have found no association between time of screening for BV and preterm birth. [178, 181, 196]

Other prospective studies have found no significant difference in rates of spontaneous preterm birth between women with and without BV. [183, 197, 198] One of these studies screened 2,929 women between 22 and 24 weeks' gestation.[198] BV by gram stain was associated with preterm birth only in multiparous women who delivered at <32 weeks gestation, with BV accounting for 11% of the attributable risk for preterm birth. [198] A prospective cohort of 2221 women screened for BV at <24 weeks' gestation using Amsel's criteria found no association between BV and risk for preterm birth (OR: 0.8; 95% CI: 0.5-1.5).[199] A similar

prospective cohort screened 1216 women at <10 weeks' gestation using Nugent's criteria and found no association between BV and preterm birth (RR: 0.9; 95% CI: 0.4-2.2). [183] Finally, a case-control study of 5,092 women screened for BV by Nugent's criteria at 26 weeks' gestation found that BV was not associated with preterm births (OR: 1.2; 95% CI: 0.5-2.4). [200] In summary, preterm birth and BV have been studied in a number of different populations. However, the information garnered from these investigations does not provide a clear picture of the role BV plays in preterm birth. While many studies report significant findings, others have been unable to show any association. Further research is needed to determine whether BV is an important risk factor for preterm birth and whether the point in pregnancy when it is diagnosed is significant (Table 7).

Table 7. Select prospective cohort studies of preterm birth and BV

Author (Year)	N	Method of BV diagnosis	Timing of BV diagnosis	Results (95% CI)
Hillier (1995)	10,397	Nugent + vaginal pH >4.5	23-26	OR 1.4 (1.1-1.8)
Gratacos (1998)	635	Gram stain	<35	RR 3.1 (1.8-5.4)
Riduan (1993)	490	Gram stain	16-20 28-32	RR 2.0 (1.0-3.9) RR 1.5 (0.7-3.0)
Thorsen (2006)	2221	Amsel	<24	OR 0.8 (0.5-1.5)
Oakeshott (2002)	1216	Nugent	<10	RR 0.9 (0.4-2.2)
Donders (2009)	1026	Modified Spiegel	First prenatal visit	OR 2.4 (1.1-4.7)

2.1.5.3 Low birth weight

Few studies have examined the link between BV and delivery of a low-birth weight (<2500g) infant. Of the four studies that have, three have shown a significant positive relationship between BV and low-birth weight, [19, 193, 201] while the fourth showed borderline results. [202] A cohort study of 3,540 pregnant women screened for BV at <20 weeks' gestation through Schmidt's method. This study found an increased risk for delivery of a low-birth weight infant (OR 1.95, 95% CI: 1.3-2.9)[19] A prospective cohort of 10,397 women screened for BV by gram stain at 23-26 weeks' gestation found that BV was related to the preterm delivery of a low-birth weight infant (OR 1.4, 95% CI:1.1-1.8).[193] This study only looked at the relation between BV and preterm delivery of a low-birth weight infant, not at low-birth weight term infants. A cross-sectional study of 49 women in idiopathic preterm labor and 38 term controls were screened for BV using Amsel's criteria at presentation for labor. Of the women in the study who delivered prematurely, 67% of the ones with BV delivered a low-birth weight infant, compared to 22% of women without BV ($p<0.0005$)[201] This study also only looked at low-birth weight infants born prematurely, not at low-birth weight term infants and also had an extremely small sample size. Lastly, a prospective study of 2,662 women screened at 17 weeks' gestation using Amsel's criteria found an increased risk of a low-birth weight infant in women with both BV and *Ureaplasma urealyticum* (OR 3.1, 1.8-5.4), but not in women with only BV (OR 0.8, 95% CI: 0.3-2.2).[202] None of these studies measured BV prior to conception or at various time point throughout pregnancy (Table 8).

Table 8. Studies of BV and low birth weight

Author (Year)	N	Study Design	Method BV of Diagnosis	Time of BV Diagnosis	Results (95% CI)
Svare (2006)	3,540	Prospective cohort	Schmidt	<20 Weeks	OR 2.0 (1.3-2.9)
Hillier (1995)	10,397	Prospective cohort	Nugent	23-26 weeks'	OR 1.4 (1.1-1.8)
Holst (1994)	87	Cross-sectional	Amsel	23-35 weeks'	P < 0.0005*
Vogel (2006)	2,662	Prospective cohort	Amsel	17 weeks'	OR 0.8 (0.3-2.2)
*OR not reported					

2.1.5.4 Small for gestational age and intrauterine growth restriction

Very little research has been done on the potential role of BV in the birth of either a small for gestation age (SGA) or intrauterine growth restricted (IUGR) infant. Only two published studies have looked at this relationship. The first, a prospective study of 2221 low-risk women screened for BV at <24 weeks' gestation using Amsel's criteria, found that women with BV had a non-significant increase in risk for having a small for gestational age infant compared to women without BV (ORa: 1.6; 95% CI: 0.7-3.1). [199] In the second, investigators conducted a matched case control study of 65 women who gave birth to a single infant with a confirmed diagnosis of IUGR and 65 controls. The authors found that genital infections, including BV, were a significant risk factor for IUGR (p=0.006). [203] This study did not break down risk further by type of infection, making it difficult to determine whether BV or another infection of interest was responsible for the increased risk. Based on the information currently available, there is little evidence that BV is associated with IUGR. It is possible that the association between BV and low birth weight is driven by the preterm births in the population. Further research is necessary

to determine whether an increased risk exists and what the possible biological mechanism involved might be.

2.1.6 Public health significance

The relationship between BV and pregnancy outcomes is unclear. While a number of studies have been conducted, results fall in both directions. A better understanding of the possible relationship between BV and these outcomes could help to dictate future screening and treatment policies for pregnant women as part of an effort to reduce spontaneous abortion, low birth weight, and preterm birth. In addition, the information would inform screening procedures in pre-pregnant women so infections could be treated and cleared prior to conception.

2.2 CONSANGUINEOUS MARRIAGE

Consanguineous marriages (CM) are common in many parts of the word. CM may be defined as a union between two individuals who are related as second cousins or closer. [27] This definition is based on the amount of genetic influence expected. Individuals who are related to a lesser degree would not be expected to share any more genetic makeup than two random people from the population.[27] Relatedness is typically expressed using the coefficient of inbreeding (F), which corresponds to the amount of inherited identical gene copies from each parent. For first cousins, this produces an F=0.0625 or 6.25% of all gene loci will be identical. [27, 204] In areas with a high degree of inbreeding, considerations need to be made for previous CMs, which may

influence whether more distant relations are included in the definition of consanguineous marriage.[204]

Prevalence of CM varies around the world, with most occurring in North Africa, the Middle East, and West Asia. [27, 204] North America, South America, most of Europe, Australia, and other developed areas have a prevalence of less than 4%. [204] The highest rates in the world are seen in the Middle East. However, several other pockets exist that have higher rates. One of these is South India, which has an estimated rate of 20-40%, depending on the specific State.[27] This is in contrast to the much lower rates found in the Northern region of the country, which are estimated to be between one and ten percent.[27] First cousin marriages comprise the largest portion of CMs, about 20-30%.[204]

Reasons for consanguineous marriages differ between geographic regions. Religion often plays a large role in deciding what types of relations are allowed to marry and different sects may have different rules. For example, the Aryan Hindus in the northern part of India do not allow marriages between close relatives and dictate that there must be a minimum of five or seven generations between relatives on the female and males, respectively, side.[27] By contrast, first cousin marriages are common and allowed by the Dravidian Hindus in the southern part of the country. These related marriages are encouraged, especially among first cousins. In addition, uncle-niece marriages are commonplace.[27] This explains the large difference in prevalence between the two regions. Sikh groups often forbid consanguineous marriage, though enforcement largely depends on the area. Judaism and Islam both allow for first cousin and double first cousin marriages, but Judaism also allows for uncle-niece relationships.[27] While religious doctrine plays a large role, the laws of the country also factor in to the prevalence. While Judaism doctrine allows for CM, the laws of many countries where these individuals live

do not allow for first cousin or closer marriages. In addition, the effects of years of related marriage have been brought to light, especially in closed communities with small gene pools, such as Amish and Ashkenazi Jews, and many of these groups have sought to ensure mixing occurs in order to protect the offspring.[27]

2.2.1 Consequences of CM

Marriage between related individuals can result in a number of adverse outcomes among their offspring. Stillbirth is a major concern and a metanalysis has shown that among first cousin marriages, a mean excess of 1.5% deaths.[22] A similar effect is seen in the number of infant deaths, with a mean 1.1% excessive deaths among first cousin offspring.[22] Consanguinity has also been shown to be associated with early childhood mortality. A 2001 study that analyzed the results of two nationally representative surveys. Using the 6,611 ever-married women ages 15 to 49 from the Pakistan Demographic and Health Survey (PDHS) 1990-1991 and the 9,485 ever-married Muslim women ages 13 to 49 who responded to the Indian National Family Health Survey (NFHS) 1992-1993, the investigators explored the association between first cousin marriages and early childhood mortality. As both surveys were designed by the same company, the sampling strategies and wording of the questions were very similar and allowed for ease of comparison. Overall, children born to first-cousin parents in India were at an increased risk of death during the neonatal period (OR: 1.3 (95% CI: 1.1-1.5)), post-neonatal period (OR: 1.2 (95% CI: 1.1-1.5)), and infant period (OR: 1.2 (95% CI: 1.1-1.5)) compared to those born to non-related parents. Additionally, children born to first-cousins were found to have an overall increased risk of death before the age of five (OR: 1.2 (95% CI: 1.0-1.4).[23] Results from analysis of the PDHS data were extremely similar, with the offspring of first cousins having an

increased risk of death during the neonatal period (OR: 1.3 (95% CI: 1.1-1.6), post-neonatal period (OR: 1.4 (95% CI: 1.2-1.8)), and infant period (OR: 1.3 (95% CI: 1.2-1.6)). Like the NFHS data, the PDHS analysis also showed an over increase in death before the age of five among children of first cousins compared to children of non-related parents.[23] Similar results were found in a study from Lebanon which showed a significant 1.8 fold increase in the risk of in-hospital mortality among the offspring of first cousin marriages compared to those of non-related marriages. They also found a significant increase in the risk of preterm birth and birth of a low birth weight infant among those in first cousin marriages ($p<0.001$). [205]

Interestingly, the overall fertility of consanguineous couples has been shown to be higher in the majority of studies.[22] It is unclear exactly why, but is possible that the increased fertility is to compensate for the higher number of losses.[22] However, it may also be due to younger age at marriage and resulting earlier first pregnancy.[24, 206, 207]

The most common association with consanguineous marriage is congenital anomalies in the offspring. Generally, the risk is considered to be 1.7-2.8% higher among offspring of first cousin marriages than among those in non-consanguineous marriages. [24-26] Most of these conditions are autosomal recessive diseases.[26] Many rare genetic conditions are seen in populations with a high degree of inbreeding that are rarely seen among non-consanguineous couple offspring. [26, 204] In developed countries, populations known to have a high degree of inbreeding or to frequently carry recessive traits often seek screening and genetic counseling prior to conception. In less developed parts of the world, where the highest degrees of consanguinity are seen, these services are often unavailable and below par.[22, 27]

Identifying adverse outcomes of consanguineous marriage is important to provide evidence-based counseling guidelines for couples seeking assistance. It may also be important in

helping to determine other causes of these outcomes, especially in areas with high levels of consanguinity. Separating out the effects of CM and other potential risk factor will assist researchers in finding potential ways minimize risk both for those in related and non-related marriages. CM and spontaneous abortion

2.2.1.1 Overview of spontaneous abortion

Spontaneous abortion is defined as the spontaneous loss of a fetus before 20 weeks' gestation. It is generally estimated the approximately 15-20% of all pregnancies end in a spontaneous abortion. [208, 209] This number is underestimated because it does not include the large number of women who miscarry during the pre-clinical phase, the time before the woman recognizes that she is pregnant. These typically occur in the first few weeks of pregnancy and end around the time the women would normally expect her menstrual cycle. As such, estimating the true percentage of pregnancies that result in spontaneous abortions is difficult. Current literature estimates that an additional 30% of pregnancies may end during this early time period, bringing the total estimate of spontaneous loss up to 45-50%. [208, 209]

Studying the causes of spontaneous abortion is extremely difficult. As previously discussed, many women do not have a recognized pregnancy prior to loss, so they are not included in most prospective studies, which often recruit women at a first prenatal visit. Prospective studies enrolling women in the pre-pregnancy stage are typically done on women receiving assisted reproductive technologies, such as IVF. [184-186] These women often have already experienced miscarriages or have been unable to become pregnant. Women undergoing assisted reproductive techniques are also from a higher socio-economic status than the general population. These issues may affect the overall generalizability of information gained from the

analysis. Further, even women who have a recognized pregnancy and know they are miscarrying do not always present to a hospital or a medical provider.

While information on exact causes and mechanisms are still poorly understood, there are a number of known and hypothesized causes and risk factors. Chromosomal abnormalities play a role in roughly half of all spontaneous abortions. These losses usually occur during the early stages of pregnancy and may account for a large percentage of the preclinical losses experienced.[209] The longer a pregnancy lasts, the more likely the cause is unrelated to chromosomal abnormalities. A related risk factor is maternal age. Women over the age of 35 are at a greater risk of spontaneous abortion than younger women. Between ages 35 and 45 the risk nearly doubles and continues to increase steadily as the woman continues to age. By age 50, there is an 80% chance that a woman will miscarry.[208, 209] This increase can mostly be associated with the increase in fetal aneuploidy. However, older women are still at an increased risk of spontaneous abortion even controlling for chromosomal abnormalities. [209] The reasons for this elevated risk are still unknown, though some researchers theorize that an increased incidence of other medical conditions, such as endocrine disorders and uterine fibroids, at older ages may be partially to blame.[208] Other theories suggest that age effects oocyte quality and may also uterine senescence. [210-213] More research is needed in order to fully understand the reasons for this increased risk among older women.

Another important consideration is environmental exposures. Lead, mercury, solvents, and radiation have all been associated with fetal loss. [214-222] In addition, smoking and second hand smoke may also as much as double a woman's chance of spontaneous abortion. [208, 209, 223, 224] This same effect may also be seen for alcohol use. [208, 209] For both smoking and alcohol, the moderate increase in risk has only been shown in a few studies and data is limited on

whether this relationship may be due to these specific teratogens or to other confounding factors. Finally, other causal factors may include infection, maternal endocrine conditions, and pharmacological drugs. In general, more research is needed to determine the biological mechanism involved in each of these processes and to determine the overall risk incurred by women exposed to these factors. [209]

2.2.1.2 Association between SAB and CM

The majority of studies looking at consanguineous marriage and spontaneous abortion are cross-sectional in nature. Often, women are asked about the nature of their relationship and then to recall their reproductive history. Studies examining this relationship have found differing results and no overall agreement has been reached. Several studies have reported a significant relationship between CM and spontaneous abortion. One case control study done in Oman looked at 141 miscarriages and compared the relatedness of the parents. 53% of cases were from consanguineous marriage and 42% were from non-consanguineous marriages. The remaining five percent were unknown.[225] No statistical comparisons were conducted to look at whether the difference in proportion were statistically significant; however, the authors did look at parental antibodies to see if there was a difference between the groups and found no statistically significant results.[225] A unique study in Nigeria looked at polygamous marriages that included both consanguineous and non-consanguineous unions. A total of 240 consanguineous couples and 229 non-consanguineous couples, for a total of 868 pregnancies, were utilized to compare rates of spontaneous abortion. Overall, the author found that spontaneous abortions were more than twice as common among consanguineous couples compared to non-consanguineous couples ($p=0.01$).[226]

There are also a number of studies who have failed to show a relationship between consanguineous marriage and spontaneous abortion. A cross-sectional study of 920 ever-married Saudi women in the City of Dammam who had experienced at least one recognized pregnancy was performed to look at whether infant outcomes were affected by the relationship of the parents. Women were asked questions about prior births, stillbirths, and spontaneous abortion, in addition to their relation to their husband prior to marriage. Overall, 52.0% were in a consanguineous relationship. Second cousin relationships had the highest rate (85.8 per 1000), followed by double first cousins (83.7 per 1000), not related (80.1 per 1000), first cousins once removed (77.3 per 1000), distantly related (71.6 per 1000) and first cousins (65.6 per 1000). However, no statistically significant difference was found between the groups.[227] While the study had a high number of women in consanguineous marriages, the numbers in some of the relation groups are quite small, which may have affected their ability to obtain adequate power in their statistical test. Further, the study only enrolled women who had ever had a recognized pregnancy. Those women having spontaneous abortions before recognition were not included in this study, possibly slanting the results. Finally, all data collected in this study were based on self-report. Whether the women properly remembered the number of spontaneous abortions or accurately identified whether they had a spontaneous abortion or a still birth is unknown. In addition, women may intentionally underreport losses due to shame or other stigmas attached to the event. In addition, early pre-clinical losses would be missed, as women would be unaware of the event. [227] Al-Awadi et al. conducted a cross-sectional study with a representative population of 5,007 Kuwaiti females ages fifteen and older who presented to one of the nation's sixteen gynecological clinics to determine whether consanguinity had an effect on prenatal and neonatal deaths. Their data showed an increase in the percent of abortions occurring in

consanguineous couples (12.04%) compared to non-consanguineous couples (11.70%), though this increase was non-significant and heavily swayed by the rate among first cousin relationships (12.44%).[228] Though this study was able to gain information on a large number of women in the population, it, like many studies, relied on self-reported data from women. Self-reported spontaneous abortion data has a number of issues associated with its use. First, women are only able to report recognized spontaneous abortions. Many women who have early miscarriages do not know they were pregnant and are therefore unaware of the loss. Second, the timing of the loss is often unknown. Inaccurate reporting of the gestational age at loss can result in misclassification bias. Finally, many women feel shame around spontaneous abortions and are unlikely to report the loss as part of a survey or interview.

2.2.1.3 Studies of CM and SAB in India

The majority of studies conducted on consanguineous marriage and reproductive outcomes have focused on the Middle East. Only five studies have reported on the effect of consanguinity in India on spontaneous abortion and stillbirth. The majority of existing data is drawn from cross-sectional studies done over large areas. An early cross-sectional study examined the Kota, an isolated tribe living in the Nilgiri Hills of Tamil Nadu. This study examined 449 couples, with 12.7% in consanguineous marriages. From both non-related and consanguineous pregnancies, roughly 8.3% reportedly ended in either spontaneous abortion or stillbirth. There was no difference between the two groups.[229] Another early cross-sectional study conducted in the North Arcot District of Tamil Nadu looked at the impact of consanguinity on fetal loss among women living in urban and rural areas.[230] A total of 20,626 women were interviewed, resulting in information on 70,161 pregnancies. Of these women, 46.9% were found to be in a consanguineous marriage, with the most common relation being first cousins, followed by uncle-

niece relationships. Overall, the investigators found that in the rural area, the fetal loss rate was significantly higher among consanguineous couples (41.5 per 1000) than among non-consanguineous couples (34.4 per 1000) ($p<0.05$). In urban areas, the opposite effect was seen, with non-consanguineous couples (70.9 per 1000) having a significantly higher rate of fetal loss than consanguineous couples (68.7 per 1000) ($p<0.05$). However, no consistent relationship was seen between degree of relatedness and rate of fetal loss. In the rural area, the highest rate of fetal loss was seen among uncle-niece marriages (45.0 per 1000), followed by beyond first cousins (43.0 per 1000), and first cousins (39.2 per 1000). In the urban area, the highest rate was among beyond first cousins relationships (78.7 per 1000), followed by uncle niece (74.0 per 1000), and first cousins (64.0 per 1000).[230] This study benefitted from direct interviews with a large population; however, the authors point out that the fetal losses captured in this data are almost all intermediate and late losses, occurring mostly after twenty weeks' gestation. As many miscarriages, especially those resulting from chromosomal abnormalities occur in the first ten weeks, the data contained in this study most likely underestimate the rate of fetal loss among all groups.

A third cross-sectional study examined 377 marriages from the area near Vellore, Andhra Pradesh. Among the relationships examined 156 (41.4%) were consanguineous, with the most common relationship being first cousins (80), followed by uncle-niece (35). Among consanguineous couples, the rate of spontaneous abortion was 4.5 per 100 pregnancies, the rate of stillbirth 1.1 per 100 pregnancies, and the overall intra-uterine loss rate 5.6 per 100 pregnancies. For non-consanguineous relationships, the rate of spontaneous abortion was 4.4 per 100 pregnancies, the rate of still birth 2.1 per 100 pregnancies, and the overall intra-uterine loss was 6.5 per 100 pregnancies. There was no significant difference in the rates of spontaneous

abortion, stillbirth, or intra-uterine loss between consanguineous and non-consanguineous couples.[231] Though this study only sampled a small number of women, the rates they demonstrated were comparable to other rates reported for the region. While the authors do not mention any issues with recall bias, women were unlikely to report early spontaneous abortions, which may be more likely to occur among consanguineous couples than among those in non-consanguineous marriages. A more recent case-control study in Pondicherry, looked at 1151 pregnancies, 751 from consanguineous couples and 400 from non-consanguineous couples.[232] Of these, a total of 7.1% and 3.7% of the consanguineous couples' pregnancies ended in spontaneous abortion or still birth, respectively. By comparison, 6% of non-consanguineous couples' pregnancies ended in spontaneous abortion and 3.7% ended in stillbirth. There was no significant difference in the rates of either pregnancy outcome between these two groups.[232] This study benefitted from drawing on a database containing information on the relatedness of the parents' marriage. However, the sample was drawn largely for the purpose of examining congenital malformations. Therefore, a large portion of the sample was drawn from parents who had at least one live birth. The process of ascertaining information on spontaneous abortion and stillbirth is unclear and may be subject to recall bias. As with many studies, early spontaneous abortions may not be recognized or reported by women to interviewers, and, therefore, not included in the analysis.

In contrast to earlier studies, a cross-sectional study utilizing data from the 1992 National Family Health Survey (NFHS) looked at data on miscarriage and consanguinity among 3,948 women in Tamil Nadu, the India state with the highest rate of marrying relatives (48.2%).[233] This study found that as degree of relatedness increased so did the likelihood the woman had experienced a miscarriage ($p=0.01$). Using logistic regression they found that the odds of

pregnancy wastage was 1.3 times higher among women who married close relatives compared to women who married distant relatives or an unrelated person, controlling for age, childhood residence, religion, caste, education status, age at marriage, and age at first birth.[233] Like previous studies, this one is subject to recall bias, since all women are asked about past experiences. In addition, no data was collected on the degree of relatedness between the couple. Additionally, spontaneous abortion and stillbirth are grouped into the same category.

All these studies required women to recall past experiences with spontaneous abortion and stillbirth. As women are unlikely to be aware of or report early spontaneous abortions, it is likely that all the captured data is from intermediate and late losses. Some studies group together all fetal loss, both spontaneous abortion and stillbirth, in order to look at total reproductive wastage. However, these two outcomes may result from different processes and consanguinity may not have the same effect on them (Table 9).

Table 9. Studies of CM and SAB in India

Author (Year)	N	Study Design	Population	% in CM	Results
Ghosh, (1979)	449 couples	Cross-sectional	Tribe, Nilgiri Hills, Tamil Nadu	12.7%	NS*
Rao (1979)	20,626 women (70,161 pregnancies)	Cross-sectional	North Arcot, Tamil Nadu	46.9%	Rural: 41.5 per 1000 (CM) vs. 34.5 per 1000 (NCM) ($p<0.05$) Urban: 68.7 per 1000 (CM) vs. 70.9 per 1000 (NCM) ($p<0.05$)
Asha Bai (1981)	377 women	Cross-sectional	Vellore, Andhra Pradesh	41.4%	4.5 per 100 (CM) vs. 4.4 per 100 (NCM) (NS)
Jai (1993)	1,151 pregnancies	Case control	Pondicherry Region	--	7.1% (CM) vs. 6% (NCM) (NS)
Sureender (1998)	3,948 women	Cross-sectional	Tamil Nadu	48.2%	1.3 %

*No rate reported

3.0 THE LONGITUDINAL INDIAN FAMILY HEALTH STUDY

The Longitudinal Indian Family Health (LIFE) Study is an ongoing collaborative project between the University of Pittsburgh and Science Health Allied Research Education (SHARE) India Research Foundation. Beginning in February of 2009, a pilot study was conducted to test protocols and procedures. This initial phase involved two of the forty villages in the Medchal Mandal region. Following completion of this test phase, recruitment for the full study began in the fall of 2010. Recruitment for the study was completed in August 2011. A total of 1,226 women from 33 villages were enrolled in the study and completed the registration visit. Of those, 932 (76.2%) are still being followed. The 294 women who are no longer being followed have been lost for a variety of reasons. A portion has been lost to follow-up or has moved away from the study villages. Others have declined further participation in the study. Finally, some women have opted for a sterilization procedure and are no longer eligible for the study. This can happen either before or after the woman has contributed a pregnancy to the study. Exact numbers for each of these categories are currently unavailable.

Study participants are contacted by staff at several time points before, during and after their pregnancy (Figure 1). After consent, participating men and women complete individual questionnaires that ask about social, behavioral, environment, and medical exposures that are of interest to study investigators. In addition, a household questionnaire is completed by one member of the couple to ascertain specific information about socio-economic status. Laboratory

sessions are scheduled for all participants. Women self-collect vaginal swabs, urine, and stool to return to the lab and have blood drawn by trained staff. Men self-collect urine and stool and also have their blood drawn by the lab team.

After enrollment, women are re-interviewed monthly to ascertain the date of their last menstrual period (LMP). Staff time follow-up calls to fall after the expected date. If the woman has not had her menstrual cycle when the team member calls, they arrange a time for the field staff to meet her and perform a urine pregnancy test. If the test is negative, the woman is called again the next month. If the test is positive, the field staff schedules her first trimester visit, which includes another questionnaire about potential exposures and an extensive reproductive history. The same specimens are collected as at enrollment. Some women enter the study already pregnant, but not yet beyond the first trimester. In this case, both the registration and first trimester questionnaire are completed, but only one set of lab samples is collected.

At the beginning of the third trimester, field staff contact the women and schedule the third trimester visit. This again consists of a questionnaire about potential exposures and collection of the same set of laboratory samples. If a woman loses a pregnancy before this time point or at any point during the pregnancy, a staff member interviews her and completes a pregnancy loss questionnaire that asks detailed questions about reason for loss, timing of loss, and potential risk factors.

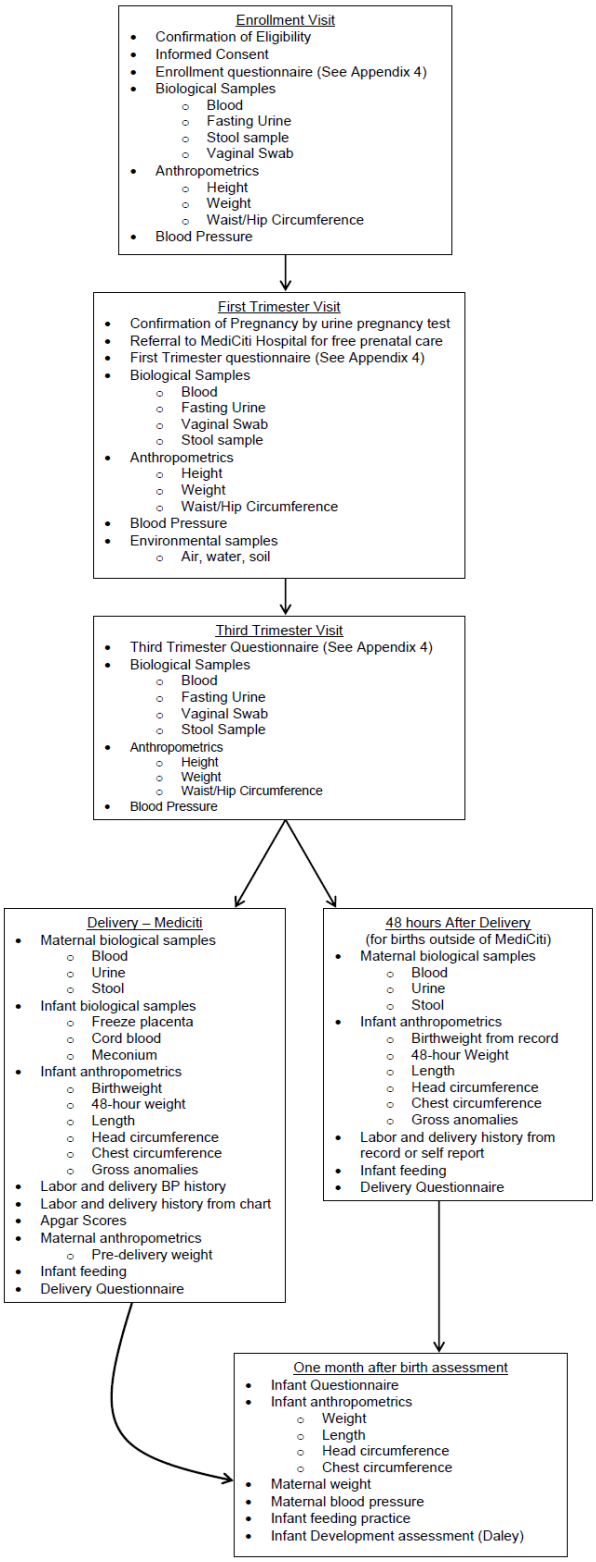

Figure 1. LIFE Study Flow Chart

The ability to collect information at delivery is dependent on where the woman delivers. Roughly half of participants deliver at MediCiti Institute of Medical Sciences, where the study is housed. Sample collection is influenced by the length of labor and complications that arise. Ideally, urine, stool, blood, and vaginal samples are taken from all women. Meconium, cord blood, and stool are all collected from the infant and a sample of the placenta is sent to the histopathology laboratory to be examined for chorioamnionitis. A chart review form that includes information on delivery complications, health of the infant, health of the mother, and medications used is completed by the attending physician or trained nurse.

Another visit is conducted at the end of the neonatal period, roughly 28 days after delivery. At this time, the same samples are again collected from the mother. A questionnaire is completed to ascertain information about the first few weeks of life. Further visits are being developed to continue to follow children through early life to study growth and development.

Women who do not undergo sterilization and are not using birth control remain in the study and are followed closely by the staff to determine the ideal time point to resume collecting LMP data. This time is determined by a number of factors, including breastfeeding practices.

The LIFE study presents a unique opportunity to look at preconception and early pregnancy exposures which may influence reproductive outcomes. Unlike studies that enroll at a first prenatal visit, the study is actively recruiting pre-pregnant women. Further, these women are not considered a planning population, since they are not focusing on conceiving, thereby changing their behavior to prepare for pregnancy. Finally, time to pregnancy in this population is short, ensuring that out sample size is large enough to gather the number of pregnancies necessary to look at these outcomes in a relatively brief period of time. Many pregnancy studies

done are conducted in developed countries, which provide little knowledge about some of the potentially unique and important exposures which are only found in the developing world. This study will provide data to inform future studies and develop public health interventions to reduce the rates of adverse outcomes in an area where the overall prevalence is high.

4.0 MANUSCRIPT 1: COMPARISON OF LABORATORY METHODS FOR IDENTIFICATION OF BACTERIAL VAGINOSIS

Manuscript in Preparation

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4.1 ABSTRACT

Background: Bacterial vaginosis (BV) is a common reproductive condition among women of childbearing age. Left untreated, BV can lead to serious reproductive sequelae and adverse birth outcomes. At MediCiti Institute of Medical Science (MIMS) in Ghanpur, Andhra Pradesh, India, the presence of clue cells in Gram stained vaginal slides as a sole criterion to diagnose BV is common in both clinical practice and research. We sought to determine whether this was a sensitive and specific way of testing for BV compared to Nugent's criteria.

Methods: Self-collected vaginal slides were collected from 883 women ages 15-35 enrolled in the Longitudinal Indian Family Health (LIFE) Study. Samples were Gram stained and analyzed for clue cells by trained laboratory staff at the Central Laboratory at MIMS. A second trained reviewer read the slides using Nugent's criteria, a quantitative laboratory method of diagnosing BV using Gram stained slides made from vaginal samples. Demographic characteristics of the population were calculated and compared using a t-test for continuous variables and chi-square test for categorical variables. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for the comparison between the two methods of BV diagnosis and agreement between the approaches was examined using the kappa statistic. Women were stratified by pregnancy status, time since last menstrual period, religion, and age to determine if differences existed in the agreement between the two methods of BV diagnosis.

Results: A total of 883 vaginal slides were analyzed. Prevalence of BV using clue cell analysis was 21.7% (95% CI: 19.0-24.5%) compared to 13.9% (95%CI: 11.6-16.2%) using Nugent's criteria. Clue cell analysis had a sensitivity of 39.8% (95% CI: 36.6-43.0%), specificity of 81.2%

(78.6-83.8%), PPV of 25.5% (95% CI: 22.7-28.4%) and NPV of 89.3% (95% CI: 87.3-91.3%) for the diagnosis of BV using Nugent's criteria.

Discussion: Clue cell analysis is an insufficient way to diagnose BV among childbearing age women. Using this method, a large proportion of the cases will be missed, potentially leading to misclassification in research studies and to serious reproductive outcomes in patient settings. Nugent's criteria, the current gold standard for BV diagnosis in research, is preferable.

4.2 BACKGROUND

Bacterial vaginosis (BV) is the most common vaginal infection among women of childbearing age. In the United States, the prevalence has been found to be 30%.[32] No population studies have been done in India, but studies have estimated that up to 39% of childbearing age women are affected.[4, 5] Left untreated, BV may lead to serious reproductive sequelae, including pelvic inflammatory disease (PID), [13-17] cervicitis [8, 10-12] and infertility. [16, 53-55] Among pregnant women, BV infection has been associated with adverse reproductive outcomes such as spontaneous abortion [20, 70, 174, 176] and preterm birth.[88, 193, 194] As up to 80% of women with BV may be asymptomatic,[32] identification of infected women can be challenging, especially in resource poor settings.

Amsel's criteria are the clinical standard for diagnosis and requires that the patient meet three out of four of the following criteria: clue cells present on >20% of epithelial cells, vaginal pH >4.5, positive amine and abnormal discharge. [62] In practice, the full criteria are often not examined by providers, leading to a number of cases being missed, even in developed countries. [66] For the purposes of research, Nugent's criteria are considered the gold standard for laboratory diagnosis. This standardized method involves quantitative scoring of three bacteria morphotypes, resulting in a score ranging from zero to 10. Women who receive scores of zero to three are considered normal, those who receive scores of four to six are classified as intermediate and those with scores of seven to 10 are considered to have BV. [71] This method has been found to have high sensitivity and specificity, as well as high inter- and intra-rater reliability. [72-74, 76]

A number of studies have examined the potential use of a limited set of Amsel's criteria or a combination of two criteria. Studies that have compared the identification of clue cells as a sole method to diagnose BV (termed clue cell analysis herein) to Nugent's criteria have found mixed results, with sensitivities ranging from 39.5-100.0% and specificities ranging from 76.0-97.0%. [34, 122, 128, 234-236] In developing countries, gynecological departments are often overburdened with women from the surrounding villages. Clue cell analysis is a fast and relatively inexpensive method of distinguishing women with BV from those without. Unlike Nugent's criteria, it does not require any specialized training and can be performed by most of the laboratory personnel. However, it is possible that relying upon using clue cell analysis misdiagnoses a number of cases that should be referred for additional care and treatment. We sought to determine the accuracy of using the presence of clue cells analysis for the diagnosis of BV in a rural South Indian population using Nugent's criteria as the gold standard.

4.3 METHODS

This study was conducted in the Central Laboratory at MediCiti Institute of Medical Sciences (MIMS) in Ghanpur, Andhra Pradesh, India, using vaginal samples collected at enrollment from women enrolled in the Longitudinal Indian Family Health (LIFE) study (n=1,226). Briefly, the LIFE Study is a longitudinal cohort study designed to study the risk factors for low birth weight among a rural South Indian population. Women were eligible to participate if they were married, living in one of the Medchal Mandal villages served by MIMS, not currently pregnant or $\leq$14 weeks' gestation and between the ages of 15-35. Women were excluded if either they or their partner had undergone a sterilization procedure, they were not planning on having any more

children or if they lived in one of the two villages with a highly transient population. At enrollment, women provided informed consent, completed a questionnaire about their current health status, and provided urine, blood, stool and vaginal samples. The LIFE study has been approved by the SHARE India Ethics committee at MIMS, Ghanpur, Andhra Pradesh, India and by the Institutional Review board at the University of Pittsburgh, Pittsburgh, PA, U.S.A.

4.3.1 Ascertainment of Demographic Information

For stratification purposes, women were considered to have been pregnant at the time of registration if they either self-reported being pregnant or had a positive urine pregnancy test at the time of enrollment. Women who were not pregnant at the time of enrollment were divided into two groups based on LMP, those who reported their LMP as $\leq$7 days prior to sample collection and those who reported their LMP as >7 days prior to sample collection. Laboratory collection was normally done within one week of women completing the questionnaire. Religion was self-reported and divided into three groups: Hindu, Muslim, and other.

4.3.2 Laboratory Methods

Vaginal samples were self-collected by women and provided to the laboratory staff. Self-collection swabs have been shown in previous studies to have high sensitivity and specificity compared to provider-collected swabs for diagnosis of BV. [81-85] Vaginal samples collected at enrollment were Gram stained and analyzed for presence of clue cells at 400x magnification by trained laboratory microbiologists in the Central Laboratory. A separate trained reviewer blinded

to the results of the clue cell analysis read the slides under 1000x magnification and quantified the morphotypes using Nugent's criteria.[71]

4.3.3 Statistical Analysis

Two comparisons of the diagnostic methods were performed. We compared women with BV by Nugent's criteria (scores 7-10) to women without BV (scores 0-6) compared to clue cell diagnosis. Second, we compared women with abnormal flora (scores 4-10) compared to women with normal flora (scores 0-3). Diagnosis of BV using clue cells was compared with the results of the Nugent scoring, which was considered the gold standard. Sensitivity and specificity, with 95% confidence intervals (95% CI), were calculated. Positive predictive values (PPV) and negative predictive values (NPP) were also calculated. A kappa value for agreement between the two methods of scoring was also calculated and assessed using the standard criteria. Stratified analysis was performed for variables that could potentially influence the accuracy of the results. Specifically, pregnancy status, age, self-reported last menstrual period (LMP) $\leq$7 days prior to swab collection.

4.4 RESULTS

4.4.1 Characteristics of the study population

A total of 883 slides were read analyzed using both Nugent's criteria and clue cell analysis. Non-pregnant women made up 78.7% of the sample (n=695). The majority, 89.2%, of women

reported their religion as Hindu (n=788), with 6.0% reporting their religion as Muslim (n=53) and 4.8% reporting another or no religion (n=42). Prevalence of BV using clue cell analysis was 21.7% (95% CI: 19.0-24.5%). The prevalence was slightly higher among non-pregnant women (23.2%; 95% CI: 20.0-26.3%) compared to pregnant women (16.49%; 95% CI: 11.1-21.8%). Using Nugent scoring, the prevalence of BV was 13.9% (95%CI: 11.6-16.2%), with higher prevalence found among non-pregnant women (15.25%; 95%CI: 12.6-17.9%) than pregnant women (9.04%; 95% CI: 86.2-94.6%). Abnormal flora (Nugent scores 4-10) was also common in our population, with a prevalence of 30.12% (95% CI: 27.1-33.1%) among the entire population, and similar rates among the pregnant (29.25%; 95% CI: 22.7-38.8%) and non-pregnant (30.36%; 95% CI: 26.9-33.8%) women (Table 13).

4.4.2 Comparison of diagnosis by clue cell analysis to Nugent's criteria

Compared to Nugent's criteria, clue cell analysis had a sensitivity of 39.8% (95% CI: 36.6-43.0%), specificity of 81.2% (78.6-83.8%), PPV of 25.5% (95% CI: 22.7-28.4%) and NPV of 89.3% (95% CI: 87.3-91.3%)(Table 14). The kappa statistic for the agreement between the two methods was 0.17, indicating low agreement ($p<0.001$). When diagnosis by clue cells analysis was compared to abnormal flora or normal flora by Nugent's criteria the sensitivity decreased to 31.2% (95% CI: 28.1-34.3%), and specificity remained similar (82.3%; 95% CI: 79.8-84.8). The PPV value increased to 43.2% (95% CI: 39.9-46.5%) and the NPV decreased to 73.5% (95% CI: 70.5-76.4%). The kappa statistic for agreement between these methods was 0.15, indicating low agreement ($p<0.001$) (Table 14).

4.4.3 Stratification by pregnancy status

When women were stratified by pregnancy status, the sensitivity of clue cell analysis compared to BV or no BV by Nugent's criteria for the diagnosis of BV among non-pregnant women was 41.5% (95% CI 37.8-45.2%). Clue cell analysis had a specificity of 80.1% (95%: 77.1-83.1%), PPV of 27.3% (95% CI: 24.0-30.6%) and NPV of 88.4% (95% CI: 86.0-90.8%). The kappa value for agreement between methods was 0.18, indicating low agreement. For pregnant women, the sensitivity of the clue cell analysis compared to Nugent's criteria was significantly lower (29.4%; 95% CI: 22.9-35.9%), as was the PPV (16.1%; 95% CI: 10.8-21.4%). Specificity (84.8%; 95% CI: 79.7-89.9%) and the NPV (92.4%; 95% CI: 88.6-96.2%) were similar. The kappa value for the agreement between methods was 0.10, indicating low agreement. Among non-pregnant women when diagnosis by clue cell analysis was compared to diagnosis of abnormal flora by Nugent's criteria the sensitivity was 33.2% (95% CI: 29.7-36.7%), the specificity was 81.2% (95% CI: 78.3-84.1%), the PPV was 43.5% (95% CI: 39.8-47.2%) and the NPV was 73.6% (95% CI: 70.2-76.9%). Among the pregnant women, the values were similar, with sensitivity of 23.6% (95% CI: 17.5-29.7%), specificity of 86.5% (95% CI: 81.6-91.4%), PPV of 41.9% (95% CI: 34.8-49.0%) and NPV of 73.2% (95% CI: 66.9-79.5%). The kappa value for agreement between the two methods was 0.12, indicating low agreement. When the area beneath the ROC curve was compared between the two groups the difference was not significant for either the comparison of diagnosis by clue cells to diagnosis of BV by Nugent's criteria ($p=0.56$) or for the comparison between diagnosis by clue cell to diagnosis of abnormal flora by Nugent's criteria ($p=0.57$) (Table 15).

4.4.4 Stratification by LMP≤7 days prior to collection

Among women who reported their LMP date as >7 days prior to vaginal swab collection the sensitivity of clue cell analysis compared to Nugent's criteria was 40.4% (95% CI: 36.4-44.4%), specificity was 80.1% (95%CI: 76.8-83.3%, PPV was 26.7% (95% CI: 23.1-30.3%), and the NPV was 88.3% (95% CI: 85.7-90.9%). The kappa value for agreement between the two methods was 0.17, indicating low agreement. Similar values for sensitivity (47.1%; 95% CI: 37.7-56.5%), specificity (80.2%; 95% CI: 72.7-87.7%), PPV (30.8%; 95% CI: 22.1-39.5%) and NPV (89.0% ; 95% CI: 83.1-94.9%) were found among women who reported their LMP to be ≤7 days prior to vaginal swab collection. The kappa value for the comparison between the two methods indicated low agreement (kappa=0.22)(Table 16).

Additional analysis comparing clue cells analysis to diagnosis of abnormal vaginal flora by Nugent's criteria showed the sensitivity to be 33.7% (95% CI: 29.9-37.5%), specificity to be 81.4% (95% CI: 78.3-84.5%), PPV to be 43.0% (95% CI: 39.0-47.0%) and the NPV to be 74.8% (95% CI: 71.4-78.3%) among women reporting their LMP as >7 days prior to collection of the vaginal swab. Overall agreement between the two methods was low (kappa=0.17). Among women who reported their LMP as ≤7 days prior to collection of the vaginal swab showed similar sensitivity(30.8% ; 95% CI: 22.1-39.5%), specificity (79.7%; 95% CI: 72.1-87.3%), PPV (46.2% ; 95% CI: 36.8-55.6%) and NPV (67.1%; 95% CI: 58.2-76.0) for the comparison between diagnosis by clue cells and diagnosis as abnormal vaginal flora by Nugent's criteria. Agreement between these two methods for this group was also low (kappa=0.11).

4.4.5 Stratification by religion

The sensitivity of diagnosis of clue cells compared to diagnosis of BV by Nugent's criteria was significantly higher among Hindus (43.0%; 95% CI: 39.5-46.5%) compared to Muslims (16.7%; 6.7-26.7%) and to women categorized as other (25.0%; 95% CI: 12.1-37.9%). The specificity was 80.5% (95% CI: 77.7-83.3%) among Hindus, 90.2% (95% CI: 82.2-98.2%) among Muslims, and 84.2% (95% CI: 73.3-95.1%) among the other group. Similar results were seen for the PPV (Hindu: 25.7%; 95% CI: 22.6-28.8%; Muslim: 33.3%; 95% CI: 20.6-46.0%; Other: 91.4%; 95% CI: 83.0-99.8%) and NPV (Hindu: 90.0%; 95% CI: 87.9-92.1%; Muslim 78.7%; 95% CI: 67.7-89.7%; Other: 91.4%; 95% CI: 83.0-99.8%). Agreement between methods for all religious groups was the low (Hindu: 0.18; Muslim: 0.08; Other: 0.07) (Table 17).

Sensitivity of clue cell analysis compared to Nugent's criteria for diagnosis of abnormal flora was lower among Muslims (14.3%; 95% CI: 5.9-23.7%) and those of other religious orientation (30.0%; 95% CI: 16.1-43.9%) as compared to Hindus (32.8%; 95% CI: 29.5-36.1%). However, the other group was not significantly different (30.0%; 95% CI: 16.1-43.9). Specificity of clue cell analysis was similar among Hindus (81.6%; 95% CI: 78.9-84.3%), Muslims (90.6%; 95% CI: 82.7-98.5%), and women categorized as other (87.5% ; 95% CI: 77.5-97.5%). Similar results were also found for the PPV and NPV (Table 17). Agreement between the methods was low for Hindus (kappa=0.15), Muslims (kappa=0.06) and the other group (kappa=0.20).

4.5 DISCUSSION

This study has shown that use of clue cells alone as a diagnostic test for BV in a rural Indian setting is inadequate compared to the gold standard, Nugent's criteria. While the specificity of the test is reasonably high, the sensitivity is too low to be considered useful in identifying women who should be treated.

The ability of clue cell analysis to diagnose BV correctly was most influenced by pregnancy status. Clue cell analysis was significantly more sensitive (41.5%; 95% CI 37.8-45.2%) among women who were not pregnant than among women who were pregnant (29.4%; 95% CI 22.9-35.9%) when compared to diagnosis of BV by Nugent's criteria (scores 7-10). Increased cervical mucus among pregnant women may make identification of clue cells more difficult. [237] We also found that clue cell analysis is more sensitive for diagnosis of BV among Hindus (43.0%95% CI 39.5-46.5%) than Muslims (16.7%; 95% CI 6.7-26.7%) when compared to diagnosis of BV by Nugent's criteria. Unmeasured cultural factors that influence vaginal flora, such as douching and ritualistic bathing rituals,[238] may create slides with few bacteria. Though the remaining bacteria can be accounted for with Nugent's criteria, it would result no clue cells.

Our study had several strengths. First, we had a large sample of women for comparison of methods, which allowed adequate power to stratify by a number of variables that were hypothesized to potentially alter the diagnostic capability of the test. Second, we were able to use the laboratory at the hospital that serves most of the population from which the participants in our study were enrolled. Use of clue cell analysis for identification and diagnosis of BV is common in this setting for both research and clinical purposes. This study allowed us to compare clue cell analysis to the gold standard test for BV in order to determine whether the laboratory's

clue cell classification is sufficient for continued use in research studies conducted in underdeveloped countries.

We did not have a measure of whether women had signs and symptoms of BV at the time of vaginal swab collection. Other studies have found that use of a single criterion from Amsel's method of diagnosis is more sensitive and specific among symptomatic women than among asymptomatic women. In addition, we were unable to compare the results of the clue cell analysis to a full clinical diagnosis by Amsel's criteria. However, studies have shown that Nugent's criteria is highly sensitive (89.1%) and sensitive (83.1%).[72]

This study suggests that while diagnosis of BV using clue cells analysis would avoid referring a large number of negative women for treatment, it would miss diagnosing a high percentage of positive patients. This is especially concerning in childbearing age women who are planning on becoming pregnant in the near future. Considering that effective and safe treatments for non-pregnant women are available in resource poor settings, identifying and treating women prior to conception should be an important part of their gynecological care and may assist in preventing adverse birth outcomes that are common in this population. For this reason, clue cell analysis should be considered an inadequate method for the diagnosis of BV and either Amsel's or Nugent's criteria should be utilized in clinical treatment and research in both developed and developing countries.

4.6 TABLES

Table 10. Comparison of Nugent scoring results to clue cell analysis

	Nugent's Score			
	Normal (scores 0-3)	Int. (scores 4-6)	BV (scores 7-10)	Total
No clue cells	508 (73.5)	109 (15.8)	74 (10.7)	691 (78.3)
Clue cells	109 (56.8)	34 (17.7)	49 (25.5)	192 (21.7)
Total	617 (69.9)	143 (16.2)	123 (13.9)	883 (100.0)

Table 11. Overall agreement between two diagnostic measures

	Sensitivity (95% CI)	Specificity (95% CI)	PPV[3] (95% CI)	NPV[4] (95% CI)	Kappa
Clue Cells compared to BV vs. no BV[1]	39.8% (36.6-43.0%)	81.2% (78.6-83.8%)	25.5% (22.7-28.4%)	89.3% (87.3-91.3)	0.1702*
Clue Cells compared to abnormal vs. normal flora[2]	31.2% (28.1-34.3%)	82.3% (79.8-84.8%)	43.2% (39.9-46.5%)	73.5% (70.6-76.4%)	0.1470*

[1] Comparison of Nugent scores 0-6 vs. 7-10
[2] Comparison of Nugent scores 0-3 vs. 4-10
[3]Positive Predictive Value
[4] Negative Predictive Value
*$p<0.001$

Table 12. Agreement between two diagnostic measures by pregnancy status

	Pregnancy Status	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Kappa
Clue Cells compared to BV vs. no BV[1]	Non-pregnant (n=695)	41.5% (37.8-45.2%)	80.1% (77.1-83.1%)	27.3% (24.0-30.6%)	88.4% (86.0-90.8%)	0.18[5]
	Pregnant (n=188)	29.4% (22.9-35.9%)	84.8% (79.7-89.9%)	16.1% (10.8-21.4%)	92.4% (88.6-96.2%)	0.10[6]
Clue Cells compared to abnormal vs. normal flora[2]	Non-pregnant (n=695)	33.2% (29.7-36.7%)	81.2% (78.3-84.1%)	43.5% (39.8-47.2%)	73.6% (70.2-76.9%)	0.15[5]
	Pregnant (n=188)	23.6% (17.5-29.7%)	86.5% (81.6-91.4%)	41.9% (34.8-49.0%)	73.2% (66.9-79.5%)	0.12[7]

[1] Comparison of Nugent scores 0-6 vs. 7-10
[2] Comparison of Nugent scores 0-3 vs. 4-10
[3]Positive Predictive Value
[4] Negative Predictive Value
[5]p<0.001
[6]p=0.07
[7]p=0.04

Table 13. Agreement of diagnostic methods by time since LMP

	Time since LMP	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Kappa
Clue Cells compared to BV vs. no BV[1]	>7 days prior to test date (n=587)	40.4% (36.4-44.4%)	80.1% (76.8-83.3%)	26.7% (23.1-30.3%)	88.3% (85.7-90.9%)	0.17[5]
	≤7 days prior to test date (n=108)	47.1% (37.7-56.5%)	80.2% (72.7-87.7%)	30.8% (22.1-39.5%)	89.0% (83.1-94.9%)	0.22[6]
Clue Cells compared to abnormal vs. normal flora[2]	>7 days prior to test date (n=587)	33.7% (29.9-37.5%)	81.4% (78.3-84.5%)	43.0% (39.0-47.0%)	74.8% (71.4-78.3%)	0.16[5]
	≤7 days prior to test date (n=108)	30.8% (22.1-39.5%)	79.7% (72.1-87.3%)	46.2% (36.8-55.6%)	67.1% (58.2-76.0%)	0.11[7]

[1] Comparison of Nugent scores 0-6 vs. 7-10
[2] Comparison of Nugent scores 0-3 vs. 4-10
[3]Positive Predictive Value
[4] Negative Predictive Value
[5]p<0.001
[6]p=0.0079
[7]p=0.1106

Table 14. Agreement of diagnostic methods by religion

	Religion	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Kappa
Clue Cells compared to BV vs. no BV[1]	Hindu (n=788)	43.0% (39.5-46.5%)	80.5% (77.7-83.3%)	25.7% (22.6-28.8%)	90.0% (87.9-92.1%)	0.18
	Muslim (n=53)	16.7% (6.7-26.7%)	90.2% (82.2-98.2%)	33.3% (20.6-46.0%)	78.7% (67.7-89.7%)	0.08
	Other (n=42)	25.0% (12.1-37.9%)	84.2 % (73.3-95.1%)	14.3% (3.8-24.8%)	91.4% (83.0-99.8%)	0.07
Clue Cells compared to abnormal vs. normal flora[2]	Hindu (n=788)	32.8% (29.5-36.1)	81.6% (78.9-84.3)	43.1% (39.6-46.6)	74.1% (71.0-77.2)	0.15
	Muslim (n=53)	14.3% (5.9-23.7)	90.6% (82.7-98.5)	50.0% (46.7-73.1)	61.7% (48.6-74.8)	0.06
	Other (n=42)	30.0% (16.1-43.9)	87.5% (77.5-97.5)	42.9% (27.9-57.9)	80.0% (67.9-92.1)	0.20

[1] Comparison of Nugent scores 0-6 vs. 7-10
[2] Comparison of Nugent scores 0-3 vs. 4-10
[3]Positive Predictive Value
[4] Negative Predictive Value

5.0 MANUSCRIPT 2: RISK FACTORS FOR BACTERIAL VAGINOSIS AMONG RURAL WOMEN IN ANDHRA PRADESH, INDIA

Manuscript in preparation

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5.1 ABSTRACT

Background: Bacterial vaginosis (BV) is a common vaginal infection among childbearing age women around the world. Risk factors for this infection are not well understood and may vary between populations. To date, no studies in India have examined a wide range of potential risk factors to look for associations with BV. Identification of potential factors would provide valuable information for screening and treatment programs.

Methods: We explored a series of potential risk factors among 658 non-pregnant and 173 pregnant women in rural India. Exposure data was ascertained through an interview with woman done at enrollment visits conducted between October 2009 and August 2011. BV status was ascertained by Nugent's criteria on Gram-stained slides made from self-collected vaginal swabs taken at the same time as the interview. To determine association with BV, crude odds ratios (OR) and 95% confidence intervals (CI) were calculated using logistic regression for each individual risk factor. Factors that were independently associated with BV at $p<0.25$ were considered for the adjusted analysis.

Results: Women who reported drinking tap water were more likely to have BV than women who reported drinking purchased water (OR_{adj} 1.4; 95% CI 0.9-2.0),.though the increase was non-significant. Non-significant increases in the odds of having BV were also seen for Muslims compared to Hindus (OR_{adj} 1.8; 95% CI 0.9-3.6).

Discussion: Among rural women in Medchal Mandal, no significant risk factors for BV were found. However, Muslim women and those who reported drinking tap water were more likely to

have BV at baseline. These trends warrant further investigation into the mechanisms behind these increases in order to inform public health screening programs.

5.2 INTRODUCTION

Bacterial vaginosis (BV) is characterized by a change in the normal vaginal flora from a majority of lactobacilli to a mix of anaerobes, *Gardnerella vaginalis*, and *Mycoplasma hominis*. [28] In the United States, BV is the most common vaginal infection, affecting roughly 30% of childbearing age women. [32] Fewer studies have been done in India to determine the prevalence and those that have been done report ranges from 4.5-64%. [34, 119, 120, 122-129] Importantly, these studies have been done mainly in large cities and have focused on high risk populations, such as sex workers or those individuals reporting to sexually transmitted infection (STI) clinics. Untreated, women with BV can develop pelvic inflammatory disease, endometritis,[6-9] cervicitis, [8, 10-12] and pelvic inflammatory disease. [13-17] Women with BV have also been shown to be more susceptible to developing sexually transmitted infections (STIs) such as Chlamydia, gonorrhea, and HIV. [56-59] In addition, BV has been associated with an increased risk of spontaneous abortion, preterm birth, low birth weight, and chorioamnionitis. [7, 11, 18, 19] Early identification and treatment of BV can prevent adverse outcomes, with standard treatment curing up to 70% of patients.[91, 156]

As early detection and treatment of BV is important for the prevention of sequelae, the identification of women at highest risk who could benefit the most from screening is important. However, the risk profile of BV remains unclear.[28, 36, 37] Though many studies have shown that sexual practices such as number of partners [130, 133] and use of condoms [132, 134, 139, 142] play a role in the development of infection, BV is not considered a sexually transmitted

infection and has been found among virginal women.[155] Numerous studies have shown several non-sexual risk factors to also play a key role in the development of BV. Evidence points toward factors such as douching,[52, 131, 135, 152, 169] stress level,[48, 50, 151] smoking,[45, 150] and hygiene. [147-149] However, there are an equal number of studies who have found no relationship between these risk factors and BV.[31, 42, 44, 52] Further research is needed to determine which factors may be key in development of BV, keeping in mind that underlying demographic and behavioral attributes of a population may impact which are most important.

As very few studies have examined risk factors for BV among Indian women,[124, 239] we sought to determine the population-based prevalence and risk factors for BV in rural Andhra Pradesh, India. Based on our knowledge of the area, we hypothesize that women with BV will be more likely to belong to a lower caste, have less education, report douching, report previous vaginal infections, and use tap water.

5.3 METHODS

5.3.1 Study design

The Longitudinal Indian Family hEalth (LIFE) Study enrolled 1,226 married women aged 15-35 from October 2009 through August 2011. Women and their husbands were eligible to participate if they lived in one of the non-transient villages that make up Medchal Mandal, were planning on having more children, neither partner was sterilized, and the woman was not currently pregnant beyond the first trimester. Husbands of potential participants were encouraged to participate in the study as well. Informed consent was obtained from all participants at the time of registration.

If the woman was under the age of eighteen, her husband was required to legally consent for her to participate and the woman provided assent.

At baseline, women were asked a series of questions about their demographics, current health status, and behavior, including questions about tobacco and alcohol consumption, water and sanitation, date of last menstrual period (LMP) and hygiene. Women were asked at enrollment whether they thought they were pregnant. Women who thought they might be pregnant were given a urine pregnancy test to confirm. For women who reported they were not pregnant or were unsure, data on the date of the participant's LMP were obtained. When women either could not remember or were more than five weeks post LMP, a urine pregnancy test was done to determine their status.

Women were also asked to provide blood, urine, stool, and vaginal samples for analysis. Vaginal samples were obtained using self-collection kits provided to enrolled participants. Trained field staff demonstrated the technique and reviewed the instructions with participants. Previous research has shown self-collected vaginal swabs to have a high sensitivity and specificity compared to provider-collected swabs when analyzed for BV. [82-86] Women collected the sample using a Dacron swab and returned the specimen to laboratory personnel in the field.

5.3.2 Laboratory Analysis

Gram-stained slides were made from vaginal samples and numbered using the participant's assigned study identification number. Slides were then read by a single observer (JE) using Nugent's criteria.[71] Women were identified as having BV if they had a score of 7-10. Normal flora was defined as a score of 0-3 and intermediate bacteria defined as a score of 4-6. The reader

was blinded to the participants' characteristics and responses to interview questions. This study protocol was approved by the Ethics Committee of the MediCiti Institute of Medical Sciences and the Institutional Review Board at the University of Pittsburgh.

5.3.3 Statistical analysis

Prevalence of BV and corresponding 95% confidence intervals were calculated in pregnant and non-pregnant women. Baseline characteristics, including age, caste, religion, employment, educational attainment, depressive symptoms, douching habits, water source, past vaginal infection, and recent urinary tract infection were compared between BV positive and negative women using the X^2 test of proportions. Fisher's exact test was substituted where necessary due to small expected values. Further stratification was done by pregnancy status and baseline characteristics reexamined. Risk factors were first examined using crude odds ratios and 95% confidence intervals. Women with BV (scores 7-10) were compared to women with normal flora (scores 0-3) and to women with either normal or intermediate flora (0-6). In addition, women with abnormal flora (scores 4-10) were compared to women with normal flora (scores 0-3). Variables that were significant ($p<.25$) in the univariate analysis in any of the models of BV or abnormal flora ($p<.25$) were included in the multivariable logistic regression model along with variables that were determined a priori to be important based on previously published literature and knowledge of cultural practices. Data were analyzed using Stata 12. [240]

5.4 RESULTS

5.4.1 Population characteristics

A total of 898 women had vaginal samples with Nugent scores from registration, 658 from women who enrolled pre-pregnancy and 173 who enrolled in their first trimester. At the time the questionnaire was administered (Table 18), women reported a mean age of 21.0 years, rated their health as very good or good (85.6%) and did not report depressive symptoms (94.2%) using the criteria established by Jeyabalan et al.[241] Participants were mostly Hindu (89.2%), belonged to a backward caste (53.2%), had a primary level education (61.3%), did not work outside of their home (75.4%), and bought canned drinking water (66.3%). About a quarter of women (26.8%) self-reported ever having a previous vaginal infection based on symptomology. Few women reported having a urinary tract infection in the previous 30 days (3.7%) or reported having ever douched (4.2%). At baseline, women who were pregnant had similar characteristics compared to women who were not pregnant (data not shown). Only education level was significantly different between the two groups, with pregnant women having a higher level of attainment (p=0.006).

5.4.2 Prevalence of BV

The overall prevalence of BV in our study was 14.1% (95% CI 11.9-16.4%), with a higher prevalence among non-pregnant women (15.3%; 95% CI 12.6-18.0%) compared to pregnant

women (9.9%; 95% CI 5.6-14.2%) (Table 19). Intermediate bacteria (Nugent scores 4-6) was also common among the population (16.1%; 95% CI 13.6-18.4%), with a higher rate among pregnant women (19.8%; 95% CI 14.1-25.5%) compared to non-pregnant women (15.0%; 95% CI 12.4-17.7). Overall, abnormal flora was present among 30.3% of the population (95% CI: 27.3-33.3%) with similar rates between pregnant (29.7; 95% CI: 23.7-36.5) and non-pregnant women (27.0-33.8).

5.4.3 Univariable analysis

In the univariable analysis (Table 20), religion (p=0.2), recent (past 30 days) self-reported urinary tract infection (UTI) (p=0.2), use of tap water compared to purchased water (p=0.1) and age (p=0.2) all met the criteria to be considered for the final multivariable models.

5.4.4 Adjusted Analysis

5.4.4.1 BV Compared to normal flora

Once adjusted for other potential risk factors, age and recent UTI did not contribute to the overall model and were not included in any of the final multivariable analysis. In the multivariable model adjusted for religion and water source (Table 21), Muslim women were more likely to have BV compared to Hindu women (OR_{adj} 1.8; 95% CI: 0.9-3.6. Women who reported their religion as other were not significantly more likely to have BV compared to Hindus (HRadj 0.63; 95% CI: 0.2-1.8). Women who used tap water were more likely to have BV at baseline than women who reported purchasing water (OR_{adj} 1.4; 95% CI: 0.9-2.0). Neither of these increases were significant.

5.4.4.2 BV compared to no BV

Comparing women with BV to those without BV, the model adjusted for religion and water source revealed that Muslim women were non-significantly more likely to have BV than Hindus (OR_{adj} 1.7; 95% CI: 0.9-3.4). There was no difference between Hindus and the other category (OR_{adj} 0.6; 95% CI: 0.2-1.9). Women who used tap water for cooking and drinking were also non-significantly more likely to have BV than women who used purchased water (OR_{adj} 1.3; 95% CI: 0.9-2.0).

5.4.4.3 Abnormal flora compared to normal flora

When women with abnormal flora were compared to those with normal flora, Muslim women (OR_{adj} 1.5; 95% CI: 0.8-2.6) and those who used tap water (OR_{adj} 1.2; 95% CI: 0.9-1.7) were more likely to have BV than Hindus and those who used purchased water, respectively. There was no difference between women who reported their religion as other compared to Hindus (ORadj 0.7; 95% CI: 0.4-1.5).

5.5 DISCUSSION

Though the relationship failed to reach significance, Muslim women and women who reported drinking tap water instead of purchased water were more likely to have BV at baseline. Unmeasured cultural practices, such as ritualistic bathing following menstruation and sexual activity,[238] may play a role in the development of BV in this population. Women who drank

tap water, as opposed to purchased water, were also non-significantly more likely to have BV. Though our study did not collect information on what source of water women used for bathing, it is likely that women drinking tap water used the same source for the purpose of cleaning themselves. Studies of water in India have shown high percentages of coliform and other bacteria.[242] A handful of studies have shown that intestinal bacteria may migrate to the vagina and cause BV.[147-149, 172]

Only a few studies in India have investigated potential risk factors for BV. The first, by Patel et al., examined a variety of reproductive tract infections (RTIs) and the influence of demographic variables, mainly related to socioeconomic status, among 2,495 women in a small community in Goa. In general, they found that women with BV were significantly more likely to be from outside the majority ethnicity group, to have fewer rooms in their home, to be illiterate, to not have access to tap water in the home, to be victims of intimate partner violence, and to have experienced hunger in the past three months.[124] The researchers did not take into account many of the behavioral factors commonly associated with BV, such as douching practices. In addition, this study did not show the increase in risk for those using tap water that was seen in our population. Women in the Goa study reported access to tap water, not whether they used it for drinking and cooking. Women in the LIFE study who purchase water may have access to tap water, but choose to use the cans instead for a variety of reasons, including knowledge of health risk associated with drinking tap water. Current data does not include a measure of whether women have access to tap water, only if they reported using it as their primary source for drinking and cooking The second study, by Thulkar et al, examined the association between recurrent vaginitis, including BV, and contraceptive use. Of the 215 women identified with BV, 2.8% reported using either an oral contraceptive pill or a copper intrauterine device (IUD),

17.2% reported using condoms, 29.3% reported no contraceptive use, and 50.7% reported having undergone tubal ligation. [239]The sample size in the study is small and represents only women with a recurrent vaginitis who presented to the study hospital in New Delhi, India and does not have include a comparison group. In addition, no potential risk factors other than contraceptive devices were taken into account. Women in our study were not asked whether they were using any contraceptive methods other than sterilization (an exclusion criteria. Based on our initial pilot studies, the rates of contraceptive use in this population are negligible and likely not an influential factor. While contraceptive practice has shown to play a role in BV development, other behavioral factors may be associated with both the type of contraceptive used and BV infection. Further studies are needed in India and within specific Indian communities to identify the risk factors that are most important to the population so that public health measures can be targeted.

This study has several strengths. First, we had a large, population based sample that is highly representative of the Medchal Mandal region of Andhra Pradesh. To our knowledge, this is the largest study of risk factors for BV in an Indian population. Second, compliance with our protocols was very high among the study population. Nearly 95% of women provided a useable self-collected vaginal swab at baseline. All of the enrolled women completed the registration questionnaire with very few missing variables. Finally, this study used Nugent's criteria to determine BV status. While this is considered the gold standard for research in the United States, it has rarely been used in Indian studies.

Our study faced several limitations. First, cultural sensitivities which prevented us from asking more probing questions about sexual practices. Information on oral sex, anal sex, sexual history, number of lifetime partners, same-sex contact and extramarital sexual encounters could

potentially be important in this population. Second, data on potential risk factors was gathered through self-report. Women were asked about past vaginal infections and recent history of UTIs. We had no way of verifying the information provided or ascertaining what sort of infection was being reported. While we have no reason to believe that participants were dishonest or misleading interviewers on any of the questions relevant to this analysis, women may have been unable to accurately recall information about their behavior in the past month or may have been afraid to answer truthfully. This is especially true for questions pertaining to past vaginal infections, depressive symptoms and douching. Third, though we considered risk factors such as vaginal douching and recent history (past month) of a UTI, the prevalence of these risk factors in our study was very low and did not provide adequate power to detect a significant difference. Studies from a variety of populations have shown douching to be a significant risk factor for BV. [115, 152] In the United States, 32% of women report douching in the past month. [136] In our study, only 4.3% of women reported ever vaginal douching, with no information on how recently the woman may have douched or the frequency of the practice. A small percent of women (3.6%) self-reported having a UTI in the past month. This data was entirely based on self-report and women were not asked whether they had been diagnosed by a healthcare provider. Finally, while we attempted to consider all variables available in the study which may be associated with BV, it is possible that potentially important risk factors relevant to this population were not included in this analysis.

BV is a serious vaginal infection that can cause adverse reproductive outcomes, including adverse pregnancy outcomes like spontaneous abortion [20, 70, 176]and preterm birth, if left untreated. Since many women are asymptomatic, screening programs rely on identifying and targeting women at the highest risk in order to provide treatment. Development of public health

programs which not only help to identify potential disease, but prevent initial infection and recurrence requires knowledge of the most important risk factors in the population. Further research into other potential risk factors in the villages is necessary in order to identify modifiable risk factors for BV. This study identified several potential groups of individuals in the Medchal Mandal villages who should be targeted for screening and treatment programs.

5.6 TABLES

Table 15. Baseline characteristic by BV status

Variable	**All (N=898)**		
	No BV N=771	BV N=127	p-value
Age (mean ± SD)	20.9 ± 3.0	21.1 ± 3.2	0.6
Religion Hindu Muslim Other	 690 (89.5) 43 (5.6) 38 (4.9)	 111 (87.4) 12 (9.5) 4 (3.2)	0.2
Caste Scheduled Backward General	 231 (30.0) 415 (58.8) 125 (16.2)	 42 (33.1) 63 (49.6) 22 (17.3)	0.7
Health Very Good/Good Average/Poor	 661 (85.7) 110 (14.3)	 108 (85.0) 19 (15.0)	0.8
Schooling None Primary Secondary+	 124 (16.1) 474 (61.5) 173 (22.4)	 24 (18.9) 76 (59.8) 27 (21.3)	0.7
Works away from home	191 (24.8)	30 (23.6)	0.8
Depressive symptoms	44 (5.7)	8 (6.3)	0.8
Past vaginal infection	206 (26.7)	35 (27.6)	0.8
Recent UTI	26 (3.4)	7 (5.5)	0.3
History of douching	33 (4.3)	5 (3.9)	0.9
Currently pregnant	173 (22.4)	19 (9.9)	0.2
Water Source Purchased Tap	 518 (67.2) 253 (32.8)	 77 (60.6) 50 (39.4)	0.2

Table 16. BV Classification by Nugent's criteria

	Normal[1] N (%)	Intermediate[2] N (%)	BV[3] N (%)	Total N (%)
N (%)	627 (69.9)	144 (16.0)	127 (14.1)	898 (100.0)

[1]Scores 0-3
[2]Scores 4-6
[3]Scores 7-10

Table 17. Results of univariable analysis

Variable	BV vs. Normal (Nugent 7-10 vs 0-3)		BV vs. No BV (Nugent 7-10 vs 0-6)		Abnormal vs. Normal flora (Nugent 4-10 vs 0-3)	
	OR (95% CI)	p-value[1]	OR (95% CI)	p-value[1]	OR (95% CI)	p-value[1]
Religion		0.2*		0.2*		0.3
Hindu	Ref		Ref		Ref	
Muslim	1.8 (0.9-3.6)		1.7 (0.9-3.4)		1.4 (0.8-2.5)	
Other	0.6 (0.2-1.8)		0.65 (0.2-1.9)		0.7 (0.4-1.5)	
Caste		0.7		0.7		0.6
Scheduled	Ref		Ref		Ref	
Backward	0.8 (0.5-1.3)		0.8 (0.6-1.3)		0.9 (0.6-1.2)	
Forward	0.9 (0.5-1.6)		1.0 (0.6-1.7)		0.8 (0.5-1.3)	
Health Status		0.9		0.8		0.9
Very good/Good	Ref		Ref		Ref	
Fair/Poor	1.0 (0.6-1.8)		1.1 (0.6-1.9)		1.0 (0.6-1.5)	
Education		0.7		0.7		0.4
None	Ref		Ref		Ref	
Primary	0.8 (0.5-1.4)		0.8 (0.5-1.4)		1.0 (0.7-1.4)	
Secondary+	0.8 (0.4-1.4)		0.8 (0.4-1.5)		0.8 (0.5-1.2)	
Works outside of Home	0.9 (0.6-1.4)	0.6	0.9 (0.6-1.5)	0.8	0.8 (0.6-1.2)	0.6
Depressive symptoms	1.1 (0.5-2.5)	0.8	1.1 (0.5-2.4)	0.8	1.13 (0.6-2.1)	0.7
History of vaginal infection	1.0 (0.7-1.5)	>0.9	1.0 (0.7-1.6)	0.8	0.88 (0.6-1.2)	0.4
Recent UTI	1.7 (0.7-4.1)	0.3	1.7 (0.7-3.9)	0.2*	1.34 (0.7-2.8)	0.4
History of douching	1.0 (0.4-2.8)	>0.9	0.9 (0.4-2.4)	0.9	1.37 (0.7-2.7	0.4
Water Source		0.1*		0.2*		0.1*
Canned	Ref		Ref		Ref	
Tap	1.4 (0.9-2.0)		1.3 (0.9-2.0)		1.25 (0.9-1.7)	
Age	1.0 (0.9-1.1)	0.9	1.0 (0.9-1.1)	0.58	1.0 (0.9-1.1)	0.2*

[1]Chi-square was used to derive p-value. Fisher's exact test was used when cell-size was less than five
*Considered for multivariable model

Table 18. Results of multivariable analysis

	BV vs. No BV		**BV vs. Normal Flora**		**Abnormal vs. Normal Flora**	
	Crude OR (95% CI)	Adjusted* OR (95% CI)	Crude OR (95% CI)	Adjusted* OR (95% CI)	Crude OR (95% CI)	Adjusted* OR (95% CI)
Religion						
Hindu	Ref	Ref	Ref	Ref	Ref	Ref
Muslim	1.7 (0.9-3.4)	1.7 (0.9-3.4)	1.8 (0.9-3.6)	1.8 (0.9-3.6)	1.4 (0.8-2.5)	1.5 (0.8-2.6)
Other	0.7 (0.2-1.9)	0.6 (0.2-1.9)	0.6 (0.2-1.8)	0.6 (0.2-1.8)	0.7 (0.4-1.5)	0.7 (0.4-1.5)
Water Source						
Canned	Ref	Ref	Ref	Ref	Ref	Ref
Tap	1.3 (0.9-2.0)	1.3 (0.9-2.0)	1.4 (0.9-2.0)	1.4 (0.9-2.0)	1.2 (0.9-1.7)	1.2 (0.9-1.7)

*Model adjusted for religion and water source

6.0 MANUSCRIPT 3: ASSOCIATION BETWEEN CONSANGUINEOUS MARRIAGE AND SPONTANEOUS ABORTION IN RURAL INDIA

Manuscript in preparation

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6.1 ABSTRACT

Background: Consanguineous marriage (CM) is a common practice in South India. For couples looking to have children, consanguinity can result in a number of adverse pregnancy and neonatal outcomes. We sought to determine whether CM was a risk factor for spontaneous abortion (SAB) in a rural South Indian population.

Methods: A total of 286 women between the ages of 15-35 with pregnancies identified at <8weeks' gestation were included in the analysis. Cox proportional hazards regression models were used to estimate the association between first-cousin marriages and spontaneous abortion, adjusting for maternal age.

Results: Overall, 19.9% of women reported being in a first-cousin marriage. Within the study population, spontaneous abortion occurred in 12.9% of pregnancies. There was a significant increase in the risk of early (≤10 weeks' gestation) spontaneous abortion (HR_{adj} 2.7, 95% CI 1.1-7.0) for women in consanguineous marriages. Similarly, there was a trend toward increased risks of late spontaneous abortions (HR_{adj} 1.2, 95% CI 0.4-3.7) or spontaneous abortions occurring at any gestational age (HR_{adj} 1.9, 95% CI 0.9-3.8) among women in consanguineous marriages, although these associations were more modest and non-significant.

Discussion: Our data show a significant increase in the risk for early spontaneous abortion, a timeframe linked with pregnancy loss due to fatal recessive disorders, among rural South Indian women in consanguineous marriages. Large prospective studies are needed to confirm our findings and determine whether they are generalizable to other populations.

6.2 BACKGROUND

Consanguineous marriage (CM) is defined as the union between two individuals who are related as second cousins or closer. [27] Globally, the prevalence of CM varies greatly. In developed countries like the United States, Western Europe, and Australia, rates are as low as 5%. [204] Much higher rates are seen in the Middle East, where studies have reported populations with CM prevalence rates of nearly 70%. [243] In India, rates differ depending on the geographic region within the country. The northern states have CM rates of between one and ten percent, while the southern states have rates between 20-60%. [27] The state of Andhra Pradesh has one of the highest rates in India, with 46% of women reporting being in a related marriage. [21] Globally, and in India, first cousin marriages are the most common form of consanguineous relationships, comprising roughly 20-30%. [204]

Marriage between related individuals has been shown to result in a number of adverse outcomes among offspring. Several studies point toward an increased risk of death among the offspring of consanguineous couples, with excess death rates up to 1.5%. [22, 23] The most commonly studied and well known association with CM is congenital anomalies. Offspring of related individuals are more likely to have uncommon autosomal recessive conditions that are rarely seen in the offspring of non-consanguineous couples. [26, 204] Depending on the population and condition, the risk is generally considered to be 1.7-2.8% higher for the children of first cousins than for those from non-related couples.

CM may also result in SAB, [226, 230, 233] although the epidemiologic study of SAB is methodologically challenging. Early miscarriages often occur before women are aware of the

pregnancy, making it difficult to rely on self-report or even clinical studies to determine the true rate. Chromosomal abnormalities are implicated in roughly 50% of early losses. [209] Sources have shown that the SAB rate is generally 15-20% of pregnancies, but this number may be as high as 50% if pre-clinical losses are included. [208, 209] In developing countries, where the majority of CMs occur, studies are even more difficult to conduct due to lack of health care infrastructure. For this reason, most studies looking at the association between CM and spontaneous abortion have been cross-sectional in nature and derived from survey data. Many of these studies have shown significant associations, [226, 230, 233] but other have had null results. [228, 229, 231, 232] Differences in rates and outcomes may differ within populations as a result of the amount of related marriage that has taken place over the years.

Our study took an active role in identifying early pregnancies as well as spontaneous abortions, providing data on SABs that might be missed using cross-sectional and self-report data. In addition, southern India, especially the state of Andhra Pradesh, is understudied in terms of both consanguineous marriage and birth outcomes. As populations, even within India, can vary greatly in terms of these variables, studies are needed to determine whether there is an increased burden in this region and to provide proper guidance for medical professionals and women looking to conceive. This paper aims to look at the association between first cousin marriages and spontaneous abortion in this area.

6.3 METHODS

6.3.1 Study Population

The Longitudinal Indian Family hEalth (LIFE) study is a prospective cohort of 1,226 childbearing age women from Medchal Mandal, a rural area outside Hyderabad, India. Women ages 15 to 35 were eligible to participate in the study if they lived in one of the non-transient villages in Medchal Mandal, planned to have more children, were not pregnant beyond the first trimester, and neither the woman nor her husband had undergone a sterilization procedure. Husbands of participating women were encouraged to enroll in the study. Demographic variables, health status, behavioral factors and environmental exposures were ascertained using questionnaires at enrollment. Women also provided urine, stool, blood and vaginal swab samples for analysis. Repeat questionnaires and biological samples were collected at the beginning of the first trimester, beginning of the third trimester, delivery and 28 days post-partum. Women identified as pregnant at enrollment were administered both registration and first trimester questionnaires, but provided only one set of biological samples for the two time points.

Field staff called or visited enrolled women monthly to determine the most recent date of the participant's last menstrual period (LMP). Women found to be more than five weeks post-LMP were provided with a urine pregnancy test. Throughout the first and second trimester, women were monitored for losses. At ten and twenty weeks' gestation, a field worker visited the woman to discuss her plans for the pregnancy and delivery and to perform a urine pregnancy test as confirmation of a progressing pregnancy. Women also reported known losses to field staff members. A pregnancy loss questionnaire was administered to all women who had a pregnancy that ended in anything other than a live birth.

This analysis was limited to women who had contributed at least one pregnancy to the study, had a singleton pregnancy, had either had a spontaneous abortion or had a pregnancy that was confirmed to be continuing past 22 weeks' gestation as ascertained at the third trimester visit. For women who had contributed more than one pregnancy to the study, only the first was used. Women who had ectopic pregnancies or induced abortions were excluded. To maximize the number of pregnancy losses identified, analyses were limited to women who had pregnancies identified at $\leq$10 weeks' gestation.

6.3.2 Related Marriage Definition

Women were asked at enrollment whether they were related to their husband prior to marriage. Those who answered in the affirmative were then asked to identify the nature of the relationship based on a provided list of common consanguineous relationships. Women who identified relationships that did not meet the standard definition of a consanguineous marriage or who were unable to provide information on the relationship were excluded. Participants who reported being in a related marriage almost exclusively reported being in a first-cousin marriage; therefore, the analysis was limited to those in non-consanguineous marriages and those in first-cousin marriages.

6.3.3 Spontaneous Abortion Definition

Spontaneous abortion was defined as a spontaneous loss occurring at <22 weeks' gestation. Last reported LMP was used to determine gestational age in the study. At the time of a loss, women were asked to estimate the date on which the loss occurred. If they were unable to pinpoint a

date, participants were prompted to approximate based on the last date that the study staff were sure the woman was pregnant. Spontaneous abortions were then classified as having occurred early (≤10 weeks' gestation) or late (11 to 22 weeks' gestation).

6.3.4 Statistical Analysis

Analyses were performed using STATA 12.0 statistical software. [240] Maternal characteristics were compared between those in related and unrelated marriages using the Student t-test for continuous variables and the chi-square test of proportions for categorical variables. In the case of low expected cell counts, Fisher's exact test was substituted for the chi-square test. We used Cox proportional hazards survival models to characterize the rate of spontaneous abortion for those in first-cousin marriages compared to those in unrelated marriages. Left truncation was used to account for variability in the gestational age at which the pregnancy was identified. Potential confounders included woman's age at the time of pregnancy, caste, self-reported health status at first trimester, educational level, parity, gravidity, and religion. Risk factors that had a p-value <0.25 from the univariable analysis were considered for inclusion in the final model. Additional analyses were performed to examine the risk of early spontaneous abortion (<10 weeks' gestation) and risk of later spontaneous abortion (10-22 weeks' gestation).

6.4 RESULTS

This study included 286 women who enrolled in the study and became pregnant between August 2009 and July 2011 (Table 1). Fifty-seven women (19.9%) reported being in first-cousin marriage. Overall, the mean age of the study population was 21.6 years. The majority of the sample was Hindu (88.8%), had a primary school education (61.5%), belonged to a backward caste (56.3%), reported their health status at the first trimester as either very good or good (87.1%), had at least one prior pregnancy (65.7%) and at least one prior live birth (60.1%). Pregnancies in this analysis were identified at a mean gestational age of six weeks. There were no significant differences between the characteristics of the women in unrelated marriages compared to those in first-cousin marriages.

Among the women in the sample, 37 (12.9%) had a spontaneous abortion, with 26 (11.4%) occurring among women in non-consanguineous relationships and 11 (19.3%) among women in first-cousin relationships (Table 2). Losses were split almost equally between the early spontaneous abortions (n=19) and late spontaneous abortions (n=18). Women in first-cousin marriages had a higher percentage of their spontaneous abortions in the early period (63.0%) compared to women in non-related marriages (46.2%).

Of the potential confounding factors investigated, only maternal age at the time of pregnancy met the criteria to be included in the final model. In the unadjusted analysis, women in first-cousin marriages were at an insignificant increased risk of spontaneous abortion compared to women in non-related marriages (HR 1.8, 95% CI 0.9-3.6) (Table 3). The risk remained non-significant once adjusted for maternal age (HR_{adj} 1.9, 95% CI 0.9-3.8). Unadjusted analyses of early spontaneous abortion showed an insignificant increase in the risk of spontaneous abortion among women in first-cousin marriage (HR 2.5, 95% CI 1.0-6.2).

However, this risk became significant once adjusted for maternal age (HR_{adj} 2.7, 95% CI 1.1-7.0). No significant increase was seen for late spontaneous abortion (HR 1.2, 95% CI 0.4-3.7; HR_{adj} 1.2, 95% CI 0.4-3.7).

6.5 DISCUSSION

Consanguineous marriage is common in many parts of the world, including South India. Our results showed a significant increase in the risk of early spontaneous abortion among women in consanguineous versus unrelated marriage, after accounting for maternal age. Similar trends were observed for late spontaneous abortions among women in consanguineous marriages, but these risks were modest and not statistically significant. This pattern is likely to reflect the lethal homozygous recessive conditions that may lead to early spontaneous abortion.[231]

Other studies on the risk of spontaneous abortion among consanguineous couples in India have shown mixed results. A study of a population in Tamil Nadu showed a significant increase in SAB [233], while others conducted in various regions of South India, excluding Andhra Pradesh, have shown insignificant [229, 231, 232] or mixed results. [230] As all of these studies have relied on retrospective data on spontaneous abortion self-reported by mothers, the studies may have missed capturing early spontaneous abortions that might go unnoticed in non-planning populations with little access to healthcare. Further, due to the nature of the studies, they were unable to separate out early and late spontaneous abortions. In addition, different geographical and ethnic groups in India have different marriage customs and may have different levels of overall relatedness. The effects of consanguineous marriage within one region may not be indicative of the risk in another as the overall relatedness of a given community influences the

prevalence of adverse conditions and outcomes. The results of this study along with previous research demonstrate a need for larger prospective studies that able to identify early pregnancies and losses among a variety of populations.

To our knowledge, this is the first study in Andhra Pradesh to prospectively look at the relationship between consanguineous marriage and spontaneous abortion. Despite the high rate of consanguineous marriage in Andhra Pradesh, little information on the degree of relatedness of couples in the area and the impact on offspring exist. Most studies of consanguineous marriage and pregnancy outcomes, including those done in other parts of India, have relied on self-reported data on past pregnancy losses collected during surveys. Our prospective design allowed us to enroll women pre-pregnancy and follow them in order to identify pregnancies, and thus pregnancy losses, early than would have been possible in pre-natal clinics.

This study had several limitations. First, despite active monitoring of women, only about a third of women had pregnancies identified at <8 weeks' gestation, and thus were eligible to be included in this analysis. Second, women were asked to self-report their pre-marital relationship to their husband. No information on ancestral relationship between the couple was available in this study. Some couples may be more related than the current analysis allows for. Future studies using blood samples may be able to determine the true degree of relatedness among participants. Finally, there may be misclassification of the outcome variable. Spontaneous abortions were ascertained through staff follow-up and self-report. It may have been several days or weeks between when the actual loss occurred and when the women became aware of the loss. For those who were near the cutoff of 22 weeks' gestation, they may have been misclassified as having had a stillbirth. To determine whether this was a potential problem in our analysis, a single fetal death variable consisting of both SABs and stillbirths (n=36) was used to repeat the analysis.

Overall, this change had little impact on our estimates and did not change the conclusion. In addition, while staff attempted to identify pregnancies as early as possible in order to have the greatest chance of observing any losses that occurred, there was still a period of time between conception and confirmation of pregnancy where some preclinical losses likely occurred.

While India, particularly the southern states, has a high rate of consanguineous marriage, little is known about the potential relationship between related marriage and spontaneous abortion. Our study showed that early spontaneous abortions were statistically more likely to occur among women in first-cousin marriages than among women in non-consanguineous marriages. Information on risk of spontaneous abortion, especially with regard to timing of losses, may help health care providers to better counsel patients who are having trouble conceiving or are having recurrent miscarriages. More prospective studies in a variety of regions and ethnic groups are needed to replicate this finding.

6.6 TABLES

Table 19. Baseline characteristic by related marriage status

Variable	Overall (n=286)	Unrelated Marriage (n=229)	First-Cousin Marriage (n=57)	p-value
Age at pregnancy	21.6	21.7	21.3	0.3
Religion				0.7
Hindu	254 (88.8)	204 (89.08)	50 (87.7)	
Muslim	17 (5.9)	14 (6.11)	3 (5.3)	
Other	15 (5.2)	11 (4.80)	4 (7.0)	
Education				0.7
None	43 (15.0)	36 (15.7)	7 (12.3)	
Primary	176 (61.5)	138 (60.3)	38 (66.7)	
Secondary+	67 (23.4)	55 (24.0)	12 (21.1)	
Caste				0.3
Scheduled Tribe/Caste	87 (30.4)	65 (28.4)	22 (38.6)	
Backward Caste	161 (56.3)	134 (58.5)	27 (47.4)	
Other	38 (13.3)	30 (13.1)	8 (14.0)	
Health Status				0.4
Very Good/Good	249 (87.1)	197 (86.03)	52 (91.2)	
Average/Poor	37 (12.9)	32 (13.97)	5 (8.8)	
Previous pregnancies				0.7
None	98 (34.3)	81 (35.4)	17 (29.8)	
1	123 (43.0)	98 (42.8)	25 (43.9)	
2+	65 (22.7)	50 (21.8)	15 (26.3)	
Previous births				0.8
None	114 (39.9)	89 (38.9)	25 (43.9)	
1	137 (47.9)	112 (48.9)	25 (43.9)	
2+	35 (12.2)	28 (12.2)	7 (12.3)	
Gestational age at time of pregnancy ascertainment (weeks)	6.0	6.0	6.1	0.6

Table 20. Cox regression models: First cousin marriage and spontaneous abortion

	Unadjusted HR (95% CI)	Adjusted HR* (95% CI)
Any spontaneous abortion	1.7 (0.9-3.6)	1.9 (0.9-3.8)
Early spontaneous abortion[1]	2.5 (1.0-6.2)	2.7 (1.1-7.0)
Late spontaneous abortion[2]	1.2 (0.4-3.7)	1.22 (0.4-3.7)

*Model adjusted for maternal age at the time of pregnancy

7.0 CONCLUSIONS AND PUBLIC HEALTH SIGNIFICANCE

The World Health Organization (WHO) estimates that 20% of the burden of disease among women is related to sexual and reproductive health. [244] In developing countries, access to screening, treatment and information can be scarce or non-existent, especially in rural areas. Though many STIs and RTIs are curable with antibiotic treatment, failure to identify these conditions early and provide adequate care can lead to serious adverse outcomes, including PID, infertility, increased risk of other infections, SAB, PTB and birth of a LBW infant.

Though much research has been done to determine risk and protective factors for RTIs like BV, this work has mainly been done in Western countries, like the United States. While this research allows for the greatest access to laboratory and healthcare infrastructure, it does not include the people who are often at the greatest risk of complications from infection. Our study sought to look at unique factors in an Indian population that might play a key role in screening and diagnosis of BV.

Proper diagnosis of BV requires adherence to strict clinical or laboratory guidelines. In underdeveloped regions, like rural Andhra Pradesh, individuals trained in these methods are often not available. Suitable alternative that are relatively fast, easy to use and accurate are needed in order to effectively screen a large number of women. Use of clue cell analysis has been proposed as an alternative to Nugent's laboratory criteria or Amsel's clinical criteria. However, this method had not previously been fully assessed for accuracy. In our comparison of

clue cell analysis to Nugent's criteria we found that while clue cells were able to accurately identify women without BV 81.2% of the time, it only correctly identified cases 39.8% of the time. As a result, we recommend that future studies be conducted to determine whether single criterion from Amsel's diagnostic criteria, such as increased vaginal pH levels or a positive whiff test, might provide better sensitivity.

Proper screening and diagnosis of large groups of people, especially in cases like BV where the majority of women are asymptomatic, can be time and resource intensive. Identification of women who are at higher risk can help to target public health programs on the individuals most likely to benefit from them. Though many studies have previously examined potential risk factors for bacterial vaginosis, they have often focused on population in the United States and Europe. As behavioral, cultural and environmental factors may all play a role in the development of BV, we sought to determine what variables might be important within a rural India population. No significant factors related to increased risk of BV at baseline were identified. However, religion and water source were borderline significant. These variables may be surrogates for unmeasured cultural practices and behavior and will be considered for future analysis.

Finally, we were interested in looking at the effect of consanguinity, specifically first cousin relationships, on spontaneous abortion. Nearly a quarter of the study population reported being married to someone they were related to prior to marriage, representing a significant portion of our participants. In an analysis adjusted for maternal age at pregnancy, we found that women in first cousin marriages were at a significantly increased risk for an early (<11 weeks' gestation) spontaneous abortion. This is hypothesized to be related to recessive genes that prevent the fetus from adapting to intrauterine life. Knowledge of risk factors can provide

valuable information to pregnant women and those seeking to become pregnant, as well as to the providers who counsel and provide care to these women.

As the LIFE study is an ongoing project, the valuable knowledge gained in these investigations will help to inform future research an analysis. PCR for detection of specific BV-related bacteria is planned for the near future and will be combined with the Nugent scores to provide a clearer picture of the characteristics of BV in the population. In addition to looking at what risk factors may be associated with these specific bacteria, we plan to look at pregnancy outcomes, such as preterm birth, spontaneous abortion, low birth weight and intrauterine growth restriction that may be associated with BV. Studies to look at factors related to spontaneous abortion are also planned and will use consanguinity as a potential confounder in the analysis.

Reproductive health combined with maternal and child health are important to the ongoing wellness of a community. In areas such as India where public health resources are scares, identification of factors that increase the risk of disease and adverse outcomes provides screening programs with the information necessary to target the groups of people who are at the greatest need. Further, public health interventions can be planned around modifiable risk factors in order to decrease the incidence of conditions within the community. These studies are first step to identifying risk and protective factors that are at play with this rural Indian community. Future studies will build upon the work presented here and develop a body of knowledge that can be drawn upon for future programs.

APPENDIX A

LIFE STUDY WOMEN'S REGISTRATION QUESTIONNAIRE

SHARE INDIA

MediCiti Institute of Medical Sciences

Ghanpur, Medchal, Ranga Reddy District-501401 A.P

LIFE PILOT STUDY 2009

Life Pilot Study Registration Visit Questionnaire-Women

R-W

IDENTIFICATION

Mandal : _____ Village : _____

Family Code : _____ Tel.No : _____

Participant's (Woman) Name : _____ Study ID : _____

Husband's Name : _____ Study ID : _____

Date of Interview : ☐☐ / ☐☐ / ☐☐☐☐
DAY MONTH YEAR

Record the Time : ☐☐ ☐☐
Hours Minutes

Interviewer's Name/ID _____

Introduction: Thank you for agreeing to respond to the questions in this questionnaire. The questions cover the following topics: your background, occupation, education, health, medical history, family history, physical activity, gender roles, sanitation, and exposure to pesticides, pollution, alcohol consumption, cigarette/bidi exposure and animal tending. We are asking each of these questions because we believe they may play a role in determining your health and may have an influence on how big your babies are when they are born. We hope that if we can find out why so many babies are so little, that we may be able to do something in the future to make sure that they are big enough when they are born.

None of this information will be shared with anyone outside of the project. We will keep your information confidential and anonymous. If you feel uncomfortable or do not want to answer any question, please say this and I (the interviewer) will then move to the next question. If you have doubts about why we are asking certain questions, please ask and I will explain the reason for the question. None of the questions are meant to offend, imply anything, or make judgments about you or your family.

పరిచయము : ఈ ప్రశ్నాపత్రములోని ప్రశ్నలకు సమాధానము ఇవ్వడానికి అంగీకరించినందుకు మీకు మా వందనాలు.
ఈ ప్రశ్నాపత్రము ద్వారా ఈ క్రింది విషయాలను గూర్చి మిమ్ములను ప్రశ్నిస్తాము: మీ కుటుంబ వివరాలు, వృత్తి, విద్య, ఆరోగ్యము, వైద్య చరిత్ర, కుటుంబ చరిత్ర, శారీరక క్రియలు, లింగపాత్రలు, పారిశుధ్యత, వాడుతున్న క్రిమి సంహారకాలు, ఇంటి పరిసరాల్లోని కాలుష్యము, మద్యపానము సేవించుట, పొగత్రాగుట లాంటి అలవాట్లు మరియు మీ పెంపుడు జంతువులు మొదలైన వాటి గురించి కొన్ని ప్రశ్నలు అడుగుతాము. ఎందుకంటే మేము అడిగే ప్రతి విషయము మీ ఆరోగ్యాన్ని నిర్ధారించుటలో పాత్ర వహిస్తుందని పాత్ర వహిస్తుందని మరియు పుట్టిన పిల్లల పరిమాణముపై ప్రభావము చూపుతుందని నమ్ముచున్నాము. శిశువులు తక్కువ పరిమాణంలో పుట్టడానికికారణాన్ని కనుక్కోగలిగితే భవిష్యత్తులో శిశువుల పరిమాణాన్ని సరి చేసేందుకు అవకాశాలుంటాయని మేము భావిస్తున్నాము.

ఈ సమాచారము ప్రాజెక్టు బయట ఎవరితోను పంచుకోము. ఈ సమాచారమును చాలా రహస్యంగా ఉంచుతాము మరియు మీ పేరు ఎక్కడచూపము. ఒకవేళ మీకు ఇబ్బందికరంగా ఉంటే, ఏదైనా ప్రశ్నకు సమాధానం ఇవ్వడం ఇష్టం లేకపోతే దయచేసి నాకు(ఇంటర్వ్యూ చేయు వారికి) తెలపండి, తప్రశ్నను వదిలి తర్వాత ప్రశ్న అడుగుతాము. ఒకవేళ మీకు ఈ ప్రశ్నలు ఎందుకు అడుగుచున్నారనే అనుమానం కలిగినట్లయితే దయచేసి నన్ను అడగండి, నేను దానికి గల కారణాలను వివరిస్తాను.
ఏ ప్రశ్న కూడా మిమ్మల్ని లేక మీ కుటుంబాన్ని లించపరచడానికి లేక మీ స్థితిగతులపై తీర్పు చెప్పడం కొరకు కాదు.

I will begin with some general questions about your background.
నేను మీకు సంబంధించిన వివరాలను సాధారణ ప్రశ్నలతో మొదలుపెడతాను.

S.NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
1. DEMOGRAPHICS వ్యక్తిగత వివరాలు			
1.1.	What is your religion? మీ యొక్క మతము ఏమిటి?	Hindu……1 Muslim……..2 Christian……3 Other_____8 (specify)	
1.2.	What is your caste and tribe? మీ యొక్క కులము ఏమి మరియు మీరు ఏ తెగకు చెందినవారు?	Caste_____ (specify) Scheduled caste….. 1 Scheduled tribe…….2 Backward caste…….3 None of the above….4	
1.3.	What is your current age? ఇప్పుడు మీ వయస్సెంత?	Age (completed years) ☐☐	
1.4	What is your date of birth? మీరు పుట్టిన తేదీ ఏమి?	☐☐ ☐☐ ☐☐☐☐ Day Month Year Don't know……..... 77	
1.5	How old were you at the time of your (current) marriage? (ప్రస్తుత) పెండ్లి నాటికి మీ వయస్సెంత?	Years ☐☐ Don't know……..... 77	
1.6	What is your date of marriage? మీ వివాహమయిన (పెళ్ళయిన) తేదీ ఏమి?	☐☐ ☐☐ ☐☐☐☐ Day Month Year Don't know……..... 77	
1.7	Before you got married, was your (current) husband related to you in any way పెళ్ళి కాక ముందు మీ (ప్రస్తుత) భర్త మీకు ఏ విధముగనైనను బంధువా?	Yes ……1 No ……2 →	**2.1**
1.8	What type of relationship was it? ఏ రకమైన బంధుత్వము?	First cousin on father's side……1 First cousin on mother's side ……2 Second cousin……3 Maternal uncle ……4 Brother-in-law……5 Other blood relative……6 Other non-blood relative ……7	
2. OCCUPATION వృత్తి **I would like to start by asking you about any work you do outside of your home, even if it's seasonal or part-time work. We would like to know about the environment in which you work.** నేను మీరు చేస్తున్న పని గూర్చి (మీ ఇంటి బయటి పని, కాలాలను బట్టి చేసే పని లేక పార్టు టైం పనులకు సంబంధించిన) ఆ చుట్టు ప్రక్కల ఉన్న వాతావరణము గురించి తెలుసుకోవాలని అడుగుతున్నాను.			
2.1	Do you work outside the home? మీరు ఇంటి బయట పని చేస్తారా ?	Yes……1 No……0 →	**3.1**

2.2	What is your occupation? మీరు ఏమి పని చేస్తారు ?	Work on own agricultural land……..1 Work on someone else land on lease…….2 Agricultural labourer……..3 Construction labourer……...4 Brick factory labour work……..5 Factory work (e.g. sewing)……6 Domestic help (someone else house)….. .7 Retail/selling things……..8 Private service……...9 Artisan/traditional caste occupation……..10 Government service……...11 Other _____12 (specify)	→ 2.6
2.3	Approximately how many days did you work in the last month (agriculture/labour) outside the home? గడచిన మాసంలో సుమారుగా ఎన్ని రోజులు ఇంటి బయట (వ్యవసాయం/కూలి) పని లోసం వెళ్ళారు?	Days ☐☐ Don't know……..... 77	
2.4	How many days in a week do you work (agriculture/labour) outside the home? మీరు వారానికి ఎన్ని రోజులు (వ్యవసాయం/కూలి) ఇంటి బయట పని చేస్తారు?	Days per week ☐☐ Don't know……..... 77	
2.5	Whenever you go to work (agriculture/labour) how long do you spend working in a day? మీరు పనికి వెళ్లిన ప్రతిసారి (వ్యవసాయం/కూలి) ఒక రోజులో ఎంత సమయం కేటాయిస్తారు?	Hours ☐☐ Don't know……..... 77	
2.6	How far is your place of work from your home? మీ ఇంటి నుండి పని చేయు స్థలము ఎంత దూరము?	≤ 1 km……1 More than 1 km, ≤ 3 km…….....2 More than 3 km, ≤ 5 km…….....3 More than 5 km……...4 Working at home……5 Don't know……..... …77	
2.7	How do you travel to your work? మీరు పనికి ఏ విధంగా ప్రయాణించి వెళ్తారు?	Walking……A Bicycle ……B Motorcycle / 2 wheeler……C Car……D Bus……...E Other _____ F (specify)	

3. EDUCATION విద్య

I would like to ask you a few questions about your education.
నేను మీ విద్యను గూర్చిన కొన్ని ప్రశ్నలు అడగాలని అనుకుంటున్నాను.

3.1.	Have you had any schooling? మీరు బడికి వెళ్లి చదువుకున్నారా?	Yes……1 No……0 →	**3.3**
3.2.	What is the highest standard you completed? మీరు ఎంత వరకు చదువుకున్నారు?	Standard ☐☐ If standard 5+ ☐ →	**3.4**
3.3.	Can you read? మీరు చదవగలరా?	Yes……1 No……0 →	**3.5**
3.4	Which languages can you read? మీరు ఏయే భాషలు చదవగలరు?	Telugu……A Hindi……B English……C Urdu……D Other _____ (specify) E If standard 5+ ☐ →	**3.6**
3.5	Can you write? మీరు వ్రాయగలరా?	Yes……1 No……0 →	**3.7**
3.6	Which languages can you write? మీరు ఏయే భాషలు వ్రాయగలరు?	Telugu……A Hindi……B English……C Urdu……D Other _____ (specify) E	
3.7	Are you currently attending any school, college, training, vocational training? ప్రస్తుతం మీరు ఏదైనా బడిలో, కాలేజీలో ట్రైనింగ్, వృత్తి విద్య లేక ట్యూటరింగ్‌లో పాల్గొంటున్నారా?	Yes _____ (specify) 1 No ……0	

4. HEALTH ఆరోగ్యము

Next, I have some general questions about your health.
తరువాత మీ ఆరోగ్యము గూర్చి కొన్ని సాధారణ ప్రశ్నలు అడుగుతాను.

4.1	Would you say your health in general is very good, good, average or poor? సాధారణంగా మీ ఆరోగ్యం ఎలా ఉందను కుంటున్నారు? చాలా బాగుందా, బాగుందా, మామూలుగా ఉందా లేక బాగా లేదా?	Very good ……1 Good ……2 Average……3 Poor……4	

The following questions are about your recent health during the past 30 days.
గడచిన 30 రోజులలో మీ యొక్క ఆరోగ్యమునకు సంబంధించిన ప్రశ్నలు ఈ క్రింద అడగబడును.

4.2	Have you had any of the following during the past 30 Days? గడచిన 30 రోజుల్లో కింద్రించి వాటిలో దేనితోనైనా బాధపడ్డారా?	YES NO NO. OF DAYS ILL	
	a. Diarrhea విరేచనాలు	1 0 ☐☐	
	b. Blood in stools మలంలో రక్తం	1 0 ☐☐	
	c. Vomiting వాంతులు	1 0 ☐☐	
	d. Asthma attacks దమ్ము	1 0 ☐☐	
	e. Respiratory infections(cough etc) శ్వాసకోశ వ్యాధులు (దగ్గు మొదలైనవి)	1 0 ☐☐	
	f. Throat infections (sore throat) గొంతువ్యాధులు (పాడి దగ్గు)	1 0 ☐☐	
	g. Urinary tract infection మూత్ర సంబంధ వ్యాధి **[prompt: burning, blood in urine, difficulty starting or stopping urination]**	1 0 ☐☐	
	h. Fever జ్వరం	1 0 ☐☐	
	i. Mental stress, depression, problems with emotions మానసిక ఒత్తిడి, కృంగిపోవుట, భావోద్రేక సమస్యలు	1 0 ☐☐	
4.3	In the past month (30 days), did you take any antibiotic or medication or pills or injection for any infection? గడచిన మాసంలో మీరు ఏదేని ఇన్ఫెక్షన్ కొరకు యాంటీ బయాటిక్ మందులు లేక సూదులు తీసుకున్నారా ?	Yes……..….1 No……..….0 Don't know……..... …77 Did not answer……..88	
4.4	*Interviewer should first write down any medications to be coded later as antibiotics* *ఇంటర్వ్యూ చేయువారు మందు పేరు ఒక ప్రశ్నను వ్రాసుకోవాలి. తరువాత అవి యాంటీబయాటిక్ మందులో కాదో తోడే చేసుకోవాలి.*	Days Taken ☐☐ Medications (specify) 1_____ 2_____ 3_____ 4_____	

In this section I am asking about vitamin deficiencies. When someone is missing certain vitamins in their diets there are three things they might experience:
- very sore and swollen tongue;
- cracks and soreness at the corners of the mouth;
- night blindness.
These symptoms of vitamin deficiency would last a long time, difficult to treat, and would probably get worse over time before getting better.
ఈ విభాగంలో నేను విటమిన్ల లోపాలను గురించి కొన్ని ప్రశ్నలు అడుగుతాను. కొంతమందికి ఆహారములో విటమిన్లు లోపించినట్లయితే వారిలో నాలుకపై పుండ్లు, పొక్కులు, నోటి చివర పగుళ్ళు రేచీకటి లాంటి లక్షణాలు కలుగవచ్చును. ఈ లక్షణాలు విటమిన్ల లోపమునకు కారణము, ఇవి చాలా కాలం ఉంటాయి మరియు చికిత్స చేయుటకు చాలా కష్టము.

4.5	Have you ever in your life had sore tongue, cracks at the corners of the mouth, night blindness that lasted more than a week and got worse over time? మీ జీవితకాలంలో మీకు ఎప్పుడైనా నాలుకపై పుండ్లు, పొక్కులు లేక రేచీకటి లాంటి లక్షణాలతో వారం కన్నా ఎక్కువ కాలం బాధపడ్డారా? Sore tongue నాలుకపై పొక్కులు Cracks at the corners of the mouth నోటి చివరలో పగుళ్ళు/పొక్కులు Night blindness రేచీకటి	అవును / Yes	కాదు / No	Did/do you take medicines? మీరు మందులు తీసుకున్నారా? Yes	No	Specify medicines మందులను వివరించండి
		1	0	1	0	
		1	0	1	0	
		1	0	1	0	
4.6	In the past month (30 days), were there any days that you were not able to do your regular duties because of illness or injury? గడచిన మాసంలో మీరు ఏదేని అనారోగ్యం లేక గాయం వల్ల మీరు మామూలుగా చేయు పనులు చేయలేకపోయారా?	Yes.....1 No.....0 →				**5.1**
4.7	How many days were you unable to do your regular duties because of injury/ illness? ఎన్ని రోజులు అనారోగ్యం / గాయం వల్ల రోజా చేయు పనులు చేయలేకపోయారు?	Injury ☐☐ Days Illness ☐☐ Days				

5. DEPRESSION అధైర్యం / కృంగుదల

These next questions are about your state of mind and mental health. With these five questions we are trying to see if you experience any of the symptoms of depression. Answering "yes" to any of these questions does not mean that you are "depressed" as it is normal for most people to feel some symptoms of depression from time to time. People may become depressed because of triggers in their lives like stress at work or problems in their home life. They may also become depressed when there is no obvious reason and everything seems fine in their life. While it is perfectly normal to feel sad or down from time to time, we are interested in whether you have experienced any of these symptoms in such a way that they overwhelm you or disrupt your regular life. For example, if a family member dies, it is normal to feel sad. But, we would like to know if you feel that kind of sadness even without an event like a death in the family or if that sadness overwhelms you to such an extent that you cannot take care of yourself or your family.

తరువాత వచ్చే ప్రశ్నలు మీ మానసిక ఆరోగ్యం గూర్చి ఉంటాయి. ఈ 5 ప్రశ్నలతో మీరు మానసిక లక్షణాలు ఏమైనా అనుభవించారా అని తెలుసుకుంటాం. ఈ ప్రశ్నలలో దేనికైనా "అవును" అని సమాధానం ఇస్తే మీరు కృంగిపోయిన స్థితిలో ఉన్నారని కాదు, కాని ఈ లక్షణాలు సర్వ సాధారణంగా ఏదో ఒక సమయాల్లో ఉంటాయి. ప్రజలు వారి జీవితంలోని ఒత్తిడి, పనిలో ఒత్తిడి లేక కుటుంబంలో సమస్యల వల్ల కృంగుదలకు గురి కావచ్చును. జీవితంలో అన్ని సౌఖ్యంగా జరుగుతున్నవ్యక్తి కూడా ఏ కారణం లేకుండానే కృంగుదలకు గురికావచ్చును. విషాదాలు లేక ఎగుడు దిగుడ్లు ఏదో సమయాల్లో ఖచ్చితంగా సర్వ సాధారణము. మీరు ఏ లక్షణాలు అనుభవించారో ఏ లక్షణాలు మీ జీవితాన్ని కలత పరిచాయో అనేది మేము తెలుసుకోవాలని ఇష్టపడుచున్నాము. ఉదా : ఒక కుటుంబంలో సభ్యుడు చనిపోతే బాధపడడం అనేది సహజం కాని మీరు అటువంటి బాధను మీ కుటుంబంలో ఎవరూ చనిపోకుండానే అనుభవిస్తున్నారా లేక అటువంటి బాధకు గురి అయి తగినంత మీ గురించి మరియు మీ కుటుంబం గురించి శ్రద్ధ తీసుకోలేకపోతున్నారా అనేది మేము తెలుసుకోవాలనుకుంటున్నాము.

5.1.	Have you had a pervasively sad or down mood or feeling of hopelessness? మీరు కృంగిపోవడం అనే భావన లేక నిరాశ భావాలు కలిగి యున్నారా? *(Probe: have you felt like things were never going to get better, that you would never be happy, that everything was going wrong and these feelings made it hard for you to function on a day to day basis?* *ప్రేరేపించు : మాకు వలెనున్నతులు ఎప్పుడూ బాగుపడవని, నేను సంతోషంగా ఉండగను, ప్రతిది తప్పు జరుగుతుంది అనే ఆలోచనలు ముమ్మిల్లి ఎక్కువగా బాధ పెట్టి రోజువారి పనులు చేసుకోవడం కష్టంగా ఉంటుందా?)*	Yes.....1 No.....0 Don't know.....77 Did not answer 88	

5.2.	Do you get less pleasure from things that you used to enjoy? మీరు సంతోషించు సమయాన తక్కువ ఆనందం పొందాలని అనిపించిందా? *(probe: have you found that things you used to like, such as watching television or spending time with friends are no longer fun for you?)* *మీరు ఇష్టపడుతో చేయు పనులు అనగా టీవి చూడడం, స్నేహితులతో గడపడం మీకు సంతోషాన్ని ఇవ్వడం లేదా?)*	Yes……1 No……0 Don't know…….....77 Did not answer ……...88	
5.3.	Have you lost weight without trying to lose weight? మీరు ఏమి ప్రయత్నం చేయకుండానే బరువు తగ్గారా? *(Probe: Are your clothes fitting differently or has anyone commented that you look thinner than before?)* *మీ బట్టలు మీకు తదుబుగా ఉన్నాయా లేక ఎవ్వరైనా మీరు ముందుకన్నా సన్నగా తనబడుతున్నారని చెప్పారా?)*	Yes……1 No……0 Don't know…….....77 Did not answer ……...88	
5.4	Do you have difficulty getting sleep, or wake up during night, or wake before everyone else wakes up? మీకు నిద్రపోవడం కష్టంగా గాని, మధ్య రాత్రిలో మెలకువ రావడం లేక అందరి కంటే ముందే నిద్ర లేవడం వంటివి వున్నాయా ?	Yes……1 No……0 Don't know…….....77 Did not answer ……...88	
5.5	Do you have suicidal ruminations? మీకు ఆత్మహత్య చేసుకోవాలనే ఆలోచనలు కల్గుతాయా? *(Probe: Have you thought about or imagined ways by which you might take your own life)* *ప్రేరేపించు : మీ జీవితాన్ని అంతం చేసుకోవాలని ఎప్పుడైనా అని పించిందా?)*	Yes……1 No……0 Don't know…….....77 Did not answer ……...88	
6. DENTAL HEALTH దంత ఆరోగ్యం : These next questions are about your teeth మీ దంత ఆరోగ్యం గూర్చి కొన్ని ప్రశ్నలు అడుగుతాను.			
6.1	Do you have any dental problems? మీకు ఏదైన దంత సమస్య ఉన్నదా ?	Yes……1 No……0 → **6.4**	
6.2	Please describe the dental problems you have experienced. దయచేసి మీ దంత సమస్యలను వివరించండి?	Bleeding gums……A Cavities (tooth pulled)……B Cavities (tooth not pulled)……C Tooth fell out (not pulled)……D Chipped or broken tooth……E Pain in teeth or gums……F Other _____G (specify)	
6.3	What did you do about these dental problems? ఈ దంత సమస్యలను గూర్చి మీరు ఏమి చేసారు?	Nothing, no help/treatment sought……A Treat at home with home remedies……B Help from village healer……C Went to dentist/dental office……D → **6.5** Other _____E (specify)	

6.4	Have you ever consulted a dentist or gone to a dental clinic? మీరు ఎప్పుడైనా దంత వైద్యుని కలిసారా లేక దంత ఆరోగ్య కేంద్రమునకు వెళ్ళారా?	Yes……1 No……0 →	**6.8**
6.5	When was the last time you saw a dentist? మీరు దంత వైద్యుని చివరిసారిగా ఎప్పుడు కలిసారు?	☐☐ ☐☐☐☐ Month Year Don't know……..... 77	
6.6	Where did you go for regular check-ups? మీరు క్రమంగా దంత పరీక్ష చేయించుకొనుటకు ఎక్కడికి వెళతారు?	Nothing, no help/treatment sought……..A Treat at home with home remedies……...B Help from village healer……C Went to dentist/dental office……D Other _____E (specify)	
6.7	How often do you have regular dental check-ups? మీరు ఎంత తరచుగా దంత పరీక్ష చేయించు కుంటారు?	Every 3 months……..1 Every 6 months……..2 Every year……...3 Every 2 years……..4 Rarely……5 Never……6	
6.8	After getting your permanent teeth, have you lost any teeth? శాశ్వత దంతాలను పొందిన తరువాత మీకు ఏమైనా దంతాలు ఊడిపోయినాయా ?	Yes……1 No……..0 Did not answer……..88 →	**6.10**
6.9	How many teeth have you lost? మీకు ఎన్ని దంతాలు ఊడిపోయినవి?	☐☐ Teeth	
6.10	How many times each day do you clean your teeth? మీరు రోజుకి ఎన్నిసార్లు మీ దంతాలను శుభ్రం చేసుకుంటారు?	☐☐ times	

6.11	What do you use to clean your teeth? మీ దంతాలను శుభ్రం చేసుకొనుటకు మీరు ఏమి వాడుతారు?		Regularly	Sometimes	Rarely
	A. Tooth brush	బ్రెష్‌తో	1	2	3
	B. Finger	చేతితో	1	2	3
	C. Cloth	బట్టతో	1	2	3
	D. Neem /margosa	వేపపుల్లతో	1	2	3
	E. Tooth paste	పేస్ట్‌తో	1	2	3
	F. Tooth powder	పొడర్‌తో	1	2	3
	G. Charcoal	బొగ్గుతో	1	2	3
	H. Salt	ఉప్పుతో	1	2	3
	I. Others	ఇతరములు	1	2	3
	_____ (specify)		Circle the spontaneous responses. Ask how often you use it – regularly, sometimes or rarely Any other way you clean your teeth? చెప్పిన దానిని మాత్రమే గుర్తించండి. ఎంత తరచుగా వాడుతారు, క్రమముగా, ఎప్పడైనా లేక అప్పడప్పడు మరియు ఇంక దేనితోనైనా శుభ్రం చేస్తారా అడగండి.		

7. PARTICIPANT'S MEDICAL AND FAMILY HISTORY పాత్రదారుని వైద్యారోగ్య అనుభవాలు :

Now I would like to ask you some questions about your medical history.
ఇప్పడు మిమ్ములను మీ వైద్యారోగ్య అనుభవాలపై కొన్ని ప్రశ్నలు అడుగుతాను

7.1	Do you suffer from any of the following? ఈక్రింది వాటిలో ఏదేని వ్యాధితో మీరు బాధపడ్డారా? ***Interviewer should try to check prescriptions if available.***	Yes	No	Age at the time of diagnosis			Do you take medicines?	
				<13 yrs	14-17 yrs	18 yrs & above	Yes	No
	Sugar disease (diabetes) షుగర్ వ్యాధి	1	0	1	2	3	1	0
	High blood pressure అధిక రక్తపోటు (హై బి.పి)	1	0	1	2	3	1	0
	Heart disease గుండె జబ్బు	1	0	1	2	3	1	0
	Asthma దమ్ము	1	0	1	2	3	1	0
	Goiter గొంతుపై కణితి	1	0	1	2	3	1	0

కుటుంబేతరుల వైద్యారోగ్య అనుభవాలు :

Now I would like to ask a few questions about your family medical history.
మీ కుటుంబ వైద్యారోగ్య అనుభవాలపై కొన్ని ప్రశ్నలు అడుగుతాను.

7.2.	Do you know the medical history / status of your parents and siblings? మీకు మీ యొక్క తల్లితండ్రుల మరియు తోబుట్టువుల వైద్యారోగ్య చరిత్ర తెలుసా?	Yes.....1 No.....0 Don't know.....77	→ 8.1
7.3.	How many sisters and brothers do you have? మీకు ఎంతమంది అక్కచెల్లెండ్రు మరియు అన్నదమ్ములు ఉన్నారు?	**Number of sisters** □□ Age of sister (yrs) #1 □□ Age of sister (yrs) #2 □□ Age of sister (yrs) #3 □□ **Number of brothers** □□ Age of brother (yrs) #1 □□ Age of brother (yrs) #2 □□ Age of brother (yrs) #3 □□	

Some diseases are hereditary, meaning that multiple members of the same family will get these diseases. For this reason we are interested in the health of your family.
కొన్ని జబ్బులు వంశపారంపర్యంగా ఉంటాయి. మీ కుటుంబంలోని అనేక మందికి ఒకే జబ్బు రావడం వంటి కారణాలన్నింటిని బట్టి మేము మీ కుటుంబ ఆరోగ్యమును గూర్చి ఆసక్తి కలిగియున్నాము.

7.4. Has anyone in your family (i.e. your mother, father, sister(s) or brother(s) ever been told by a doctor or nurse that they had the following indicated in the Table.
మీ కుటుంబంలో ఎవరికైనా అనగా మీ తల్లికిగాని తండ్రికిగాని అక్కచెల్లెండ్రులకు గాని, అన్నదమ్ములకు గాని ఈ క్రిందివి ఉన్నవని డాక్టరు గాని నర్స్‌గాని ఎప్పుడైనా చెప్పినారా?

	Sugar disease?			High blood pressure?			Heart problems?		
	Yes	No	DK	Yes	No	DK	Yes	No	DK
Mother	1	0	77	1	0	77	1	0	77
Father	1	0	77	1	0	77	1	0	77
Brother	1	0	77	1	0	77	1	0	77
# of brothers	□□			□□			□□		
Sisters	1	0	77	1	0	77	1	0	77
# of sisters	□□			□□			□□		

7.5	Was your mother or were your sister(s) ever told they had toxemia, pre-eclampsia, or high blood pressure during pregnancy? మీ తల్లికిగాని, అక్క,చెల్లెండ్రులకుగాని గర్భధారణ సమయాల్లో ఎప్పుడైనా మూర్ఛవ్యాధిగాని, అధిక రక్తపోటు గాని ఉండి ఉన్నాయని చెప్పినాలా?	Yes No Mother 1 0 Sister(s) 1 0 How many sisters? ☐☐ Don't Know.....77	
8. BIRTH HISTORY జనన చలత్ర :			
The following questions are about your birth history. మీ పుట్టుకను గూర్చి ఈ క్రింది ప్రశ్నలు అడుగుతారు			
8.1.	Were you born prematurely, that is, more than 3 weeks early? మీరు నెలలు నిండక ముందే జన్మించారా? అంటే 3 వారాలు తంటే ముందే?	Yes.....1 No.....2 Don't know..... 77	→ 8.3
8.2	How many weeks early were you born? మీరు ఎన్ని వారాల ముందు పుట్టినారు?	Weeks ☐☐ Don't know..... 77	
8.3	What was your birth weight when you were born? *Record weight in kilograms.* మీరు పుట్టినప్పుడు ఎంత బరువుతో పుట్టినారు?	KG ☐.☐☐ Don't know..... 77	→ 8.5
8.4	Is this birth weight from memory or from a medical card? మీ బరువు మీకు జ్ఞాపకముండినదా లేక మెడికల్ లకార్డులో నున్నదా?	Memory.....1 Medical card.....2	
8.5	What was your size at birth? మీరు పుట్టినప్పుడు ఎంత పెద్దగా ఉన్నారు?	Large/chubby/big baby.....1 Normal size baby..... 2 Small.....3 Very small.....4 Don't know..... 77	
8.6	Were you a twin or triplet మీరు కవల పిల్లలా ?	Not twin/triplet.....1 Twin.....2 Triplet.....3 Other _____ 4 (specify)	→9.1
8.7	Were you and your twin identical or fraternal? మీరు కవలలయితే మీరు మీ తోబుట్టువు ఒకే పోలికగా ఉంటారా లేక వేరువేరుగా ఉంటారా? ***Probe – if they were identical in looks, mark identical*** ఒకవేళ వారు ఒకే పోలికతో ఉంటే '1' గుర్తించండి	Identical.....1 Fraternal.....2 Don't know..... 77	
9. REPRODUCTIVE HEALTH సంతానోత్పత్తి ఆరోగ్యము These next questions are about your menstrual cycle and reproductive health తరువాత వచ్చే ప్రశ్నలు మీ యొక్క రుతుచక్రము మరియు సంతానోత్పత్తి ఆరోగ్యము గూర్చి			
9.1.	How old were you when you had your first menstrual period? మీరు మొదటిసారి పుష్పవతి/పెద్దమనిషి అయినప్పుడు మీ వయస్సెంత?	Age (Years) ☐☐ Don't know..... 77	

9.2	Have you recently missed a menstrual period? ఈ మధ్య కాలంలో మీకు నెలసరి తప్పినదా?	Yes……1 No……0 Don't know……..... .77	
9.3	What was the first day of your last menstrual period? గత నెలసరిలో మొదటిరోజు ఏమిటి ? Use events of the past month like festivals to probe for first day of last menstrual period గత నెలలో జరిగిన పండుగలు మొదలగు వాటిపై లోతుగా అడిగి నెలసరిలో మొదటిరోజు తెలుసుకోవాలి.	☐☐ ☐☐ ☐☐☐☐ Day Month Year Don't know…… 77	
9.4.	When do you usually have your menstrual period each month? మామూలుగా ప్రతి నెల మీ నెలసరి ఎప్పుడు వస్తుంది?	According to calendar (date)……1 New moon……2 Before half moon……..3 Full moon……4 Does not come at predictable times……..5 Comes rarely……6 Never had a menstrual period…….. 7 Don't know……77 Did not answer…….. 88	
9.5	Have you ever used the Sunday/Monday tablets to delay your period? మీరు ఎప్పుడైనా నండే, మండే బిళ్లల్ని వాడినారా?	Yes……..1 No…… 0 Not aware of tablets……77	→ 9.7
9.6	How many *Sunday/Monday* tablets have you taken in the past three months? గత మూడు నెలల్లో ఎన్ని నండే, మండే బిళ్లల్ని తీసుకున్నారు?	Tablets ☐☐	
9.7	Have you ever had a vaginal infection or vaginal problems? (*Thella batta, Erra batta*) మీకు ఎప్పుడైనా యోని సంబంధిత అంటు వ్యాధి లేక యోనికి సంబంధించిన సమస్యగాని వచ్చినదా? (తెల్లబట్ట, ఎర్రబట్ట)	Yes……1 No……0 Don't know……..... .77	
Some women use a technique known as douching. By douching, we mean putting a substance into your vagina for routine cleansing. To clean regularly with soap and water on the outer part of the vagina is not douching. కొంతమంది స్త్రీలు డౌచింగ్ అనే టెక్నిక్ వాడుతారు. డౌచింగ్ అనగా యోనిలో ఒక పదార్థం పెట్టి వాడుకగా శుభ్రం చేయుట కాని తరచుగా సబ్బు నీటితో యోని చుట్టు ప్రక్కల శుభ్రం చేసుకొనుట డౌచింగ్ కాదు.			
9.8	Do you put a substance into your vagina for routine cleansing? మీకు యోనిలో ఏదైనా పదార్థమును పెట్టి శుభ్రం చేసే వాడుక/అలవాటు ఉన్నదా? ***Probe to make sure that she is not saying yes because she cleans regularly with soap and water.***	Yes……1 No……0 Don't know……..... .77	

9.9	Did a doctor or medical professional ever instruct you to use something to clean inside your vagina? మీకు డాక్టర్‌గాని, నర్స్‌గాని ఎప్పుడైనా యోనిని శుభ్రం చేసుకొను విధానములు మీకు సూచించారా?	Yes.....1 No.....0 Don't know 77	→ 10.1
9.10	In the past 30 days, how many days have you douched? గడచిన 30 రోజుల్లో మీరు ఎన్ని రోజులు డౌచింగ్ చేసారు?	Days ☐☐ Don't know.....77 Did not answer 88	
9.11	What type of products do you use to douche? మీరు ఏ రకమైన పదార్థములతో డౌచింగ్ చేస్తారు?	Douching product sold in stores.....A Vinegar.....B Betadine / iodine.....C Scented vaginal product.....D Household cleansers_____E (specify) Home made _____F (specify) Don't know.....77 Did not answer 88	
10. PREGNANCY AND FERTILITY PREFERENCES గర్భధారణ మరియు ఫలదీకరణ ప్రాధాన్యతలు Now would like to ask you about pregnancy and desired number of children. ఇప్పుడు మిమ్మల్ని గర్భాధారణ మరియు మీకు ఎంత మంది పిల్లలు కావాలనుకుంటున్నారు అనే విషయాలను గూర్చి అడుగుతాను.			
10.1	Are you pregnant now? మీరు ఇప్పుడు గర్భిణీగా ఉన్నారా?	Yes.....1 No .....0 Don't know.....77 Did not answer.....88	→ 10.3
10.2	How many weeks pregnant are you? మీరు ఎన్ని వారాల గర్భవతి?	Weeks ☐☐	→ 10.4
10.3	Are you trying to become pregnant? మీరు గర్భము కొరకు ప్రయత్నిస్తున్నారా?	Yes.....1 No.....0 Don't know.....77	→ 10.4
10.3a	Since how long you are trying for pregnancy ? మీరు ఎంతకాలం నుండి గర్భము కొరకు ప్రయత్నిస్తున్నారు?	Weeks..... ☐☐ or Months ..... ☐☐ or Years ..... ☐☐	
10.4	Have you and your husband been together in the past week (7 days)? మీరు, మీ భర్త, గతవారము (ఏడురోజులు) దాంపత్యంలో కలిసి ఉన్నారా?	Yes.....1 No.....0 Did not answer 88	→ 10.6
10.5	How many days have you been together in the past week (7 days)? గతవారములో (7 రోజుల్లో) మీరు ఎన్ని రోజులు దాంపత్యంలో కలిసారు?	Days ☐☐	

11.4.	Please describe your daily schedule or routine for a typical day during the past week. ***Prompt: As the woman describes her routine, probe for amount of time spent doing each activity.*** దయచేసి గత వారంలో ప్రత్యేకంగా ఒక రోజులో మీరు చేయు పనులు వివరించండి. స్త్రీ తన రోజువారి పనులలో ప్రతి పని కొరకు ఎంత సమయం కేటాయిస్తుందో ఈ క్రింది పట్టికలో వ్రాయండి.

	Morning (before 12.00 noon)		**Afternoon (12.00 noon-4.00pm)**		**Evening (4.00pm onwards)**	
Domestic work						
		Time spent		**Time spent**		**Time spent**
a) Sweeping	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes
b) Cooking	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes
c) Serving food to the household members	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes
d)Washing utensils	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes
e)Washing clothes/laundry	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes
f) Care of children	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes
g) Care of animals	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes
Other Work						
h)Farming/Gardening	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes
i) Labour, construction work	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes
j) Stitching	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes	**Yes 1** **No 0**	☐☐ Hours ☐☐ Minutes

k) Other_____ (specify)	**Yes** 1 **No** 0	☐☐ Hours ☐☐ Minutes		**Yes** 1 **No** 0	☐☐ Hours ☐☐ Minutes		**Yes** 1 **No** 0	☐☐ Hours ☐☐ Minutes
Resting								
l) Nap	**Yes** 1 **No** 0	☐☐ Hours ☐☐ Minutes		**Yes** 1 **No** 0	☐☐ Hours ☐☐ Minutes		**Yes** 1 **No** 0	☐☐ Hours ☐☐ Minutes
m) Watch TV	**Yes** 1 **No** 0	☐☐ Hours ☐☐ Minutes		**Yes** 1 **No** 0	☐☐ Hours ☐☐ Minutes		**Yes** 1 **No** 0	☐☐ Hours ☐☐ Minutes

COOKING వంట

11.5.	How much rice do you cook each day? (Include morning, midday, evening meals) రోజుకి ఎన్ని కేజీల బియ్యం వండుతారు? (ఉదయం, మధ్యాహ్నం మరియు రాత్రి భోజనాలు కలుపుతూ)	☐☐ kg Don't know……77	
11.6.	Where do you buy or obtain the rice that you cook for your family? మీ కుటుంబానికి వంట చేయుటకు కావలసిన బియ్యము ఎక్కడ నుండి కొనుక్కుంటారు / తెచ్చుకుంటారు?	Family's own paddy……A Local / neighbor's paddy……B Buy from grocer……C Buy from government/ ration shop……D Other_____E (specify)	
11.7.	Where is the cooking done at your house? మీ ఇంట్లో వంట ఎక్కడ చేస్తారు?	In the designated kitchen……1 In common room used for other activities…..2 Outside house……3 → **11.10** Others _____(specify) 4	
11.8.	Is there a vent above the cooking area? మీరు వంట చేయు స్థలము పైన కిన్నము ఉన్నదా?	Yes……1 No……0 Don't know……77	
11.9.	Is there a window that you open near the cooking area? మీరు వంట చేయు స్థలము దగ్గర కిటికీ ఉన్నదా?	Yes……1 No……0 Don't know……77	
11.10.	On everyday, how long are you exposed to cooking fires? How many hours? ప్రతి రోజు వంట చేయునప్పుడు మీరు మంటకు ఎంతసేపు గురి అవుతారు?	Hours ☐☐	
11.11.	What type of fuel does your household mainly use for cooking? మీరు వంట చేయుటకు ఏరకమైన ఇంధనం వాడతారు?	Firewood / crop residuals……1 Electricity…… 2 LPG/Natural gas……3 Gobar or bio gas……4 Kerosene……5 Coal/Lignite……6 Charcoal……7 Straw/shrubs/grass……8 Dung / dung cake……9 Other _____10 (specify)	→ **12.1**

11.12.	Who fetches the firewood? కట్టెలు ఎవరు తెస్తారు?	Wife (life participant).....1 Husband (life participant)..... 2 Children.....3 Other_____4 (specify)	→ 12.1
11.13.	How do you go to fetch firewood? కట్టెలు తెచ్చుకొనుటకు ఎలా వెళతారు?	Walking.....1 Bicycle.....2 2-wheeler.....3 Other.....4 (Specify)	→ 11.15
11.14.	How far do you have to walk to fetch firewood? మీరు కట్టెలు తెచ్చుకొనుటకు ఎంత దూరము నడచి వెళ్ళవలసి ఉంటుంది?	≤1 KM.....1 1-3 KM.....2 More than 3KM..... 3 Don't know.....77	
11.15.	How often each week does you fetch firewood? ప్రతి వారము మీరు ఎంత తరచుగా కట్టెలు తెస్తారు?	Times per week ☐☐ Don't know.....77	
11.16.	How long does it take to go there, collect firewood, and come back in one trip? ఒక ట్రిప్పుకి కట్టెలు తీసుకొని రావడానికి ఎంత సమయం పడుతుంది?	Minutes ☐☐ Don't know.....77	
12. WATER SOURCES నీరు - ముఖ్యాధారములు			
12.1.	Do you use same water for drinking and cooking? మీరు త్రాగడానికి మరియు వంటకి ఒకే రకమైన నీటిని వాడతారా ?	Same water.....1 Different water.....2	→ 12.3
12.2.	What is the source of water you use for drinking and cooking? మీరు త్రాగడానికి మరియు వంటకి వాడే నీటిని ఎక్కడ నుండి తెచ్చుకుంటారు?	Purchased cans.....1 Piped (tap).....2 Bore hand pump.....3 Open well.....4 Others_____5 (Specify)	→ 12.5 → 12.6
12.3.	What is the source of water you use for drinking? మీరు త్రాగడానికి వాడే నీరు ఎక్కడ నుండి తెచ్చు కుంటారు?	Purchased cans.....1 Piped (tap).....2 Bore hand pump.....3 Open well.....4 Others_____5 (Specify)	
12.4.	What is the source of water you use for cooking? మీరు వంట చేయడానికి వాడే నీరు ఎక్కడ నుండి తెచ్చుకుంటారు?	Purchased cans.....1 Piped (tap).....2 Bore hand pump.....3 Open well.....4 Others_____5 (Specify)	

12.5.	If cans are purchased, how much do you spend? క్యాన్స్ కొనుక్కున్నట్లయితే మీకు ఎంత ఖర్చవుతుంది?	Rs._____ 5litres can……1 10 litres can……..2 15 litres can……..3 20 litres can……..4 Free Supply …….5	
12.6.	How do you prepare water for drinking? మీరు త్రాగు నీటిని ఏ విధంగా శుభ్రం చేస్తారు?	No preparation……1 Boiling……..2 Chlorination……3 Use water Filter……4 Use Electronic Purifier……5 Sedimentation…… 6 Other_____7 (specify)	
12.7.	Do you yourself travel to fetch water for your household? మీ ఇంటికి కావలసిన నీరు మీరే వెళ్ళి తెచ్చుకుంటారా?	Yes……1 No……0 →	12.12
12.8.	How far do you travel to fetch water? మీరు నీళ్ళు తెచ్చుకొనుటకు ఎంత దూరం ప్రయాణించి వెళతారు?	≤ 1km…….. 1 1-3 km…….. 2 > 3 km……3 Don't know…….. 77	
12.9.	How do you travel to fetch the water? మీరు నీళ్ళు తెచ్చుకొనుటకు ఏ విధంగా ప్రయాణించి వెళ్తారు?	Walking……..1 Bicycle……2 Motorcycle……3 Other _____4 (specify)	
12.10.	How long does it take to go there, get water, and come back in one trip? ఒకసారి వెళ్లి నీళ్ళు తీసుకొని వచ్చుటకు ఎంత సమయం పడుతుంది?	Minutes ☐☐☐ Don't know…….. 77	
12.11.	How often do you fetch water and how much do you carry each time? మీరు ఎంత తరచుగా నీళ్ళు తెచ్చుకుంటారు మరియు ప్రతిసారికి ఎన్ని నీళ్ళు తెస్తారు?	Trips per day ☐☐ Containers per trip ☐☐ Liters in container #1 ☐☐ Liters in container #2 ☐☐	
12.12.	How is water collected from the source into the carrying container? మీరు నీరు లభించే స్థలం నుండి పాత్రలోకి ఏ విధంగా పట్టుకుంటారు?	Piped direct, no carrying container……1 Direct from source into carrying container (i.e. buy water and it is put directly into your can)……..…2 Cloth covers collecting container as a filter……3 One container is used to transfer water from source to carrying Container……..4 Other method_____ 5 (specify)	

12.13.	How is drinking water stored? మీరు త్రాగు నీటిని ఏ విధంగా నిల్వ చేస్తారు?	In the container……1 Pots……2 Drums / cans……3 Overhead tank……4 Other_____ 5 (specify)	→ 12.16
12.14.	How frequently do you clean/change the carrying container? ఎంత తరచుగా మీరు నీటిని నిల్వ చేయు పాత్రను శుభ్రం చేస్తారు? *Probe – if cleaned when it becomes empty, ask how often that happens.*	Daily……1 Once a week……2 Fortnightly……3 Once a month……4 Other _____5 (specify)	
12.15.	If you clean/wash water containers, how do you wash? ఒకవేళ నీటిని నిల్వ చేయు పాత్రలను శుభ్రపరిస్తే దేనితో శుభ్రపరుస్తారు?	Washing powder or soap……1 Rinsed with water only……2 Other _____3 (specify)	→ 12.20
12.16.	**Overhead tank**: మిద్దెపైన ట్యాంక్ What is your indication that the storage container should be cleaned? నీటిని నిల్వ చేయు ట్యాంక్‌ను శుభ్రపరచుటకు గల సూచన లేమి?	No indication……1 Smell……2 Taste of water……3 Color of water……4 Other _____5 (specify)	
12.17.	How frequently is the storage container cleaned? ఎంత తరచుగా మీరు ట్యాంక్‌ను శుభ్రం చేస్తారు?	Weekly……1 Monthly……2 Bi-monthly……3 Every six months……4 Yearly……5 Other _____6 (specify)	
12.18.	How long does the water in the storage container last? ట్యాంక్‌లో నున్న నీరు ఎంతకాలం వస్తుంది?	1 week……1 2 weeks……2 More than 2 weeks……3	
12.19.	For what purposes do you open the water storage container? మీరు ట్యాంక్‌ను ఎందు కోసము తెరుస్తారు?	Never……1 To check the water level……2 To fill water……3 To clean container……4 Other_____5 (specify)	
12.20	Is the quantity of water you collect sufficient for your family needs? మీరు నిల్వ చేసిన నీరు మీ కుటుంబానికి సరిపోతుందా?	Yes……1 No _____ 0 (specify)	

13. PESTICIDES AND POTENTIAL EXPOSURE క్రిమి సంహారకాలు మరియు ప్రభావము

Pesticides include many types of chemicals used to repel, kill, or control unwanted weeds, insects, rodents, fungi, or bacteria. They are used on crops, animals, buildings, or roads.

చాలా రకాల రసాయనికాలను గృహ కీటకాలను వెళ్ళగొట్టుటకు, చంపుటకు, కలుపు మొక్కలను, అలికట్టుటకు, పురుగులను, ఎలుకలను, పుట్టగొడుగులను లేక బాక్టీలయాను అదుపు చేయుటకు, జంతువులకు,పంటలకు, ఇళ్ళు మరియు రోడ్ల నిర్మాణాలకు వాడుతాం

13.1	Do you or does your household mix, apply, spray, process, or use pesticides? మీరు పురుగుల మందును కలపడం, చల్లటం లేక పురుగుల మందును వాడుతారా ?	Yes 1 No 0 → **14.1** Don't know 77 → **14.1**	
13.2	Where do you or your household mix, apply, spray, process or use pesticides? పురుగుల మందు ఎక్కడ చల్లుతారు ?	In the house A Courtyard B Farm C Work place D Other _____ E (specify)	
13.3	Who use these pesticides? పురుగుల మందు ఎవరు చల్లుతారు?	Wife(participant).....1 Husband.....2 Other family members.....3 Servants/workers.....4 Govemment people.....5 Others_____6	→ **13.6**
13.4	When you use/apply the pesticide product(s) at work, do you wear any protective clothing? క్రిమి సంహారకాలు వాడుతున్నప్పుడు మిమ్మల్ని మీరు కాపాడుకొనుటకు ఏమైనా రక్షకాలు ధరిస్తారా?	Yes.....1 No.....0 → **13.7**	
13.5	What do you wear? మీరు ఏమి ధరిస్తారు?	Face mask.....1 Gloves.....2 Other_____ 3 (Specify)	
13.6	What are the names of the pesticides you (your household) have used in the past three months at work? గడచిన 3 నెలల్లో మీరు పని చేయు స్థలంలో వాడిన క్రిమి సంహారకాల పేర్లు తెలపండి ?	_____ _____ _____ (specify) Don't know.....77	

13.7	How often the following pesticides used in the past three months at your work? గడచిన 3 నెలల్లో ఎంత తరచుగా మీరు పని చేయు స్థలంలో ఈ క్రింది క్రిమి సంహారకాలను వాడారు ?						
Type of pesticides క్రిమి సంహారకాల రకములు		Once per day	Several times per week	Once per week	Once per month	Once in three months	Never
a. Insecticides to kill bugs/mosquitoes దోమలను, నల్లులను చంపు క్రిమిసంహారకాలు		1	2	3	4	5	6
b. Herbicides (weed killer) కలుపు మొక్కలను చంపు మందులు		1	2	3	4	5	6
c. Rodenticides to kill rats and mice ఎలుకలను మరియు చిట్టెలుకలను చంపు రోడెంటిసైడ్స్		1	2	3	4	5	6
d. Fungicides to kill mold or fungus ఫంగస్‌ను చంపు ఫంగీసైట్స్		1	2	3	4	5	6
e. Bactericides to kill bacteria బాక్టీరియాను చంపు బాక్టీలీసైట్స్		1	2	3	4	5	6
f. Other (describe): _____ ఇతరములు (Specify)		1	2	3	4	5	6

14. CIGARETTE / BIDI EXPOSURE సిగరెట్ / జీడీ ప్రభావము			
Present Smoking ప్రస్తుతం పొగత్రాగుట			
14.1.	Do you smoke tobacco-related products (like cigarettes, bidis, hookah etc.) now? ఇప్పుడు మీరు పొగాకుకి సంబంధించిన పదార్థములు (అనగా సిగరెట్లు, జీడీలు, హుక్కా మొదలైనవి) త్రాగుతున్నారా?	Yes (cigarettes)……1 No……0 Did not answer…….. 88 →	**14.4**
14.2.	How long have you been smoking at least 3 times per week? ఎప్పటి నుండి మీరు వారానికి కనీసం 3సార్లు పొగ త్రాగుతున్నారు?	☐☐ Years smoking bidi If <1 year ☐☐ months smoking	
14.3.	How many cigarettes or bidi or other tobacco-related product do you currently smoke per day? ప్రస్తుతం మీరు రోజుకి ఎన్ని సిగరెట్లు లేక జీడీలు లేక పొగాకుకి సంబంధించిన పదార్థములు త్రాగుతున్నారు?	☐☐ Cigarettes per day ☐☐ Bidi per day ☐☐ Other tobacco related product per day If Q.14.1 is YES →	**14.9**
Past Smoking గతంలో పొగత్రాగుట			
14.4.	Have you ever, in the past smoked cigarettes or bidi or other tobacco-related product, but now you do not smoke? ప్రస్తుతం మీరు పొగత్రాగక పోయినా గతంలో ఎప్పుడైనా సిగరెట్లు, జీడీ లేక ఇతర పొగాకుకి సంబంధించిన పదార్థములు త్రాగేవారా?	Yes (cigarettes)……1 Yes (bidi)……2 Yes (other product) ……3 No……0 Did not answer…….. ..88 →	**14.9**

14.5.	Have you ever in the past smoked at least 3 times per week? గతంలో ఎప్పుడైనా మీరు వారానికి 3సార్లు పొగ త్రాగేవారా?	Yes (cigarettes).....1 Yes (bidi).....2 No.....0 Did not answer..... 88	
14.6.	How long did you smoke before you quit? మీరు మానివేయడానికి ముందు ఎంతకాలం అలా త్రాగారు?	☐☐ Years smoking bidi If <1 year ☐☐ months smoking	
14.7.	What year did you quit? ఏ సంవత్సరములో మీరు మానివేసారు?	☐☐☐☐ Year ☐☐ Month If participant quit this year, which month?	
14.8.	When you were smoking, how many cigarettes or bidi or other tobacco-related product did you smoke on a typical day? మీరు పొగత్రాగేటప్పుడు ఒక రోజుకి ఎన్ని సిగరెట్లు లేక బీడీలు లేక ఇతర పొగాకుకి సంబంధించిన పదార్థములు త్రాగేవారు?	☐☐ Cigarettes per day ☐☐ Bidi per day ☐☐ Other tobacco related product per day	
Exposure to smoking from others (passive smoking) ఇతరులు పొగ త్రాగుటం వలన కలిగే ప్రభావము			
14.9.	Have you ever exposed to tobacco smoke (like cigarette, bidi, hookah etc.) in your home because of smoking by others? మీ ఇంట్లో ఇతరులు పొగ త్రాగుట వలన మీరు ఎప్పుడైనా (సిగరెట్, బీడీ, చుట్ట లేక పైపు) పొగకి గురి అయ్యారా?	Yes .....1 No.....0 → **14.13**	
14.10.	About how many hours per day are you exposed to this smoke in your home because of smoking by others? మీ ఇంట్లో ఇతరులు పొగ త్రాగడం వలన రోజుకి ఎన్ని గంటలు ఆ పొగను పీల్చుకుంటారు?	☐☐ Hours per day	
14.11.	About how many hours per week are you exposed to this smoke in a small space other than your home, such as friends or relatives homes or at work, because of smoking by others? మీ ఇంట్లో కాకుండా మీ స్నేహితుల మరియు బంధువుల ఇంట్లో ఉన్న కొంచెం స్థలములో ఇతరులు పొగత్రాగడం వలన వారానికి ఎన్ని గంటలు ఆ పొగను పీల్చుకుంటారు?	☐☐ Hours per week	
14.12.	Which of the others living in your house smoke tobacco-related products (like cigarettes, bidi, hookah etc.)? మీ ఇంట్లో ఎవరు (సిగరెట్, బీడీ, హుక్కా మొదలైన) పొగను త్రాగుతారు?	Husband A Father/Father-in-law B Mother/Mother-in-law C Brother/Brother-in-law D Other person _____ (specify) E	

14.13.	Do you chew anything on a regular basis (e.g. pan masala, betel leaves, betel nuts, tobacco) మీరు క్రమముగా ఏమైనా నములుతారా ? (ఉదా: తమల పాకు, పాన్‌మసాల, వక్కపొడి, పొగాకు మొదలైనవి)	Yes……..1 No……..0 Did not answer……..88	→15.1
14.14.	What do you chew? మీరు ఏమి నములుతారు?	Pan masala……..A Betel leaves…… B Betel nuts……C Tobacco……..D Other_____ E (specify)	
14.15.	How often do you chew? మీరు ఎంత తరచుగా నములుతారు?	More than once a day……..1 Once a day……..2 Every few days……...3 Once per week……4 Occasionally……5	
15. INCENSE ధూపము			
15.1.	Do you burn incense in your house? మీ ఇంట్లో అగరుబత్తిని వెలిగిస్తారా?	Yes……1 No……0	→ 15.3
15.2.	How often do you burn incense in your house? ఎంత తరచుగా అగరుబత్తిని వెలిగిస్తారు?	Daily or most days……..1 More than once a week, not daily…2 Rarely, only on special days…….3	
15.3.	Do you burn mosquito coils in your house? మీ ఇంట్లో దోమ చుట్టను వెలిగిస్తారా? (దోమలను తలమేందుకు పొగచుట్ట)	Yes……1 No……..0	→ 16.1
15.4.	How often do you burn mosquito coils in your house? ఎంత తరచుగా దోమచుట్లను వెలిగిస్తారు?	Daily or most days……..1 More than once a week, not daily…2 Rarely……..3	
16. CLEANING PRODUCTS శుభ్రపరిచే వస్తువులు			
16.1.	Do you clean the walls or floors of the house? మీరు మీ ఇంటి గోడలను లేక నేలను శుభ్రపరుస్తారా?	Yes……1 No……..0	→17.1
16.2.	How often you clean the walls or floor by using the following products? ఈ క్రింది నున్న వాటిలో దేనితో మీ ఇంటి గోడలను, నేలను ఎంత తరచుగా శుభ్రం చేస్తారు?		

Cleaning product శుభ్రపరిచే వస్తువులు	Once a day	A few times per week	Once per week	Once per month	Once per season	Once a year
a. Water only నీటితో	1	2	3	4	5	6
b. Ash బూడిద	1	2	3	4	5	6
c. Detergent, bar soap or washing soda డిటర్జెంట్ లేక సబ్బు లేక సోడాతో	1	2	3	4	5	6
d. Chlorine bleach క్లోరిన్	1	2	3	4	5	6
e. Cow dung ఆవు పేడతో అలకడం	1	2	3	4	5	6
f. phenyl ఫినాయిల్	1	2	3	4	5	6
g. Other_____ ఇతరములు (specify)	1	2	3	4	5	6

17. ALCOHOL CONSUMPTION మద్యపానము

17.1.	Do you drink any alcohol or alcoholic beverages? మీరు ఏదైనా మద్యపానమును సేవిస్తారా?	Yes……1 No……0 Did not answer……88	→ 18.1
17.2.	If yes, which of the following types of alcohol do you drink, and how often? అవును అయితే, ఏరకమైన మద్యపానమును మీరు త్రాగుతారు మరియు ఎంత తరచుగా త్రాగుతారు?		

Type of beverage మద్యపాన రకములు	Yes అవును	No కాదు	More than once a day రోజుకి ఒకసారి కంటే ఎక్కువ	Once a day రోజుకి ఒకసారి	A few times each week వారానికి కొన్నిసార్లు	About once per week వారానికి ఒకసారి	Once per month నెలకి ఒకసారి	Rarely (3-4 times per year) ఎప్పడైనా సం॥ కి సార్లు	No. of bottles or sachets at one sitting ఒకసారికి ఎన్ని సీసాలు లేక ప్యాకెట్లు
a. Beer బీర్	1	0	1	1	1	1	1	1	☐☐
b. Wine వైన్	1	0	1	1	1	1	1	1	☐☐
c. Toddy కల్లు	1	0	1	1	1	1	1	1	☐☐
d. Whisky విస్కీ	1	0	1	1	1	1	1	1	☐☐
e. Arrack (Govt. liquor) సారాయి	1	0	1	1	1	1	1	1	☐☐
f. Other _____ (specify) ఇతరములు	1	0	1	1	1	1	1	1	☐☐

18. VEHICLES AND POLLUTION EXPOSURE వాహనములు మరియు కాలుష్య ప్రభావము

18.1.	How often did you ride in/on a vehicle (yours or someone else's) in the past three months? గడచిన 3 నెలల్లో మీరు ఎంత తరచుగా (మీది లేక ఇతరుల వాహనము) పై ప్రయాణం చేసారు?	Daily……1 Weekly……2 Monthly……3 Never……4	

19. ANIMALS AND LIVESTOCK జంతువులు మరియు పశువులు			
19.1.	Do you tend animals outside the home (i.e. on a farm)? మీరు ఇంటి బయట ఏమైనా జంతువులను పెంచుతున్నారా? (ఉదా : పొలములో)	Yes.....1 No.....2 →	**End**
19.2.	What animals and how many do you tend? ఏ జంతువులు మరియు ఎన్నింటిని పెంచుతున్నారు?	Yes / No / Number	
	a. Dogs	1 0 ☐☐	
	b. Cats	1 0 ☐☐	
	c. Goats...	1 0 ☐☐	
	d. Sheep	1 0 ☐☐	
	e. Chicken or ducks	1 0 ☐☐	
	f. Buffaloes and cows	1 0 ☐☐	
	g. Donkeys	1 0 ☐☐	
	h. Other ----------(Specify)	1 0 ☐☐	

THANK THE RESPONDENT FOR HER CO-OPERATION AND REASSURE HER ABOUT THE CONFIDENTIALITY OF HER ANSWERS

RECORD THE TIME: _____ Hour ☐☐
Minutes ☐☐

APPENDIX B

LIFE STUDY FIRST TRIMESTER QUESTIONNAIRE

SHARE INDIA
MediCiti Institute of Medical Sciences
Ghanpur, Medchal, Ranga Reddy District-501401 A.P

LIFE PILOT STUDY 2009
Life Pilot Study 1st Trimester Visit Questionnaire

IDENTIFICATION

Mandal : _____ Village : _____

Family Code : _____ Contact Tel: _____

Husband's Name : _____ Study ID: _____

Wife's Name : _____ Study ID: _____

Date of Interview : ☐☐ / ☐☐ / ☐☐☐☐
DAY MONTH YEAR

Record the Time : ☐☐ ☐☐
Hours Minutes

Interviewer's Name/ID: _____

Introduction: Thank you for agreeing to respond to the questions in this questionnaire. The questions cover the following topics: your current health, your pregnancy history, your exposure to cigarettes and your mental health. We are asking each of these questions because we believe they may play a role in determining your health and may have an influence on how big and healthy your babies are when they are born. We hope that if we can find out why so many babies are so little, that we may be able to do something in the future to make sure that they are big enough when they are born.

None of this information will be shared with anyone outside of the project. We will keep your information confidential and anonymous. If you feel uncomfortable or do not want to answer any question, please say this and I (the interviewer) will then move to the next question. If you have doubts about why we are asking certain questions, please ask and I will explain the reason for the question. None of the questions are meant to offend, imply anything, or make judgments about you or your family.

పరిచయము : ఈ ప్రశ్నాపత్రములోని ప్రశ్నలకు సమాధానము ఇవ్వడానికి అంగీకరించినందుకు మీకు మా వందనాలు. ఈ ప్రశ్నాపత్రము ద్వారా ఈ క్రింది విషయాలను గూర్చి మిమ్ములను ప్రశ్నిస్తాము. మీ ప్రస్తుత ఆరోగ్యము, మీ గర్భారోగ్య చరిత్ర, పొగత్రాగుటలాంటి అలవాట్లు మరియు మీ మానసిక ఆరోగ్యము మొదలైన వాటి గురించి కొన్ని ప్రశ్నలు అడుగుతాము. ఎందుకంటే మేము అడిగే ప్రతి విషయము మీ ఆరోగ్యాన్ని నిర్ధారించుటలో పాత్ర వహిస్తుందని మరియు పుట్టిన పిల్లల పరిమాణముపై ప్రభావము చూపుతుందని నమ్ముచున్నాము. శిశువులు తక్కువ పరిమాణంలో పుట్టడానికి కారణాన్ని కనుక్కోగలిగితే భవిష్యత్తులో శిశువుల పరిమాణాన్ని సరి చేసేందుకు అవకాశాలుంటాయని మేము భావిస్తున్నాము.
ఈ సమాచారము ప్రాజెక్టు బయట ఎవరితోను పంచుకోము. ఈ సమాచారమును చాలా రహస్యంగా ఉంచుతాము మరియు మీ పేరు ఎక్కడ చూపము. ఒకవేళ మీకు ఇబ్బందికరంగా ఉంటే, ఏదైనా ప్రశ్నకు సమాధానం ఇవ్వడం ఇష్టం లేకపోతే దయచేసి నాకు (ఇంటర్వ్యూ చేయు వారికి) తెలపండి. ఆ ప్రశ్నను వదలి తర్వాత ప్రశ్న అడుగుతాము. ఒకవేళ మీకు ఈప్రశ్నలు ఎందుకు అడుగుచున్నారనే అనుమానం కలిగినట్లయితే దయ చేసి నన్ను అడగండి, నేను దానికి గల కారణాలను వివరిస్తాను. ఏ ప్రశ్న కూడా మిమ్మల్ని లేక మీ కుటుంబాన్ని కించపరచడానికి లేక మీమీ స్థితిగతులపై తీర్పు చెప్పడం కొరకు కాదు.

1. Background			
1.1	What was the first day of your last menstrual period? మీ గత నెలసరిలో మొదటి రోజు ఏమిటి ? Use events of the past month like festivals to probe for first day of last menstrual period గత మాసంలోని పండుగలులాంటి ముఖ్య సంఘటనలను ఉపయోగించండి	☐☐ Day ☐☐ Month ☐☐☐☐ Year Don't know..... -77 Don't know Day..... -78 Don't know Month..... -79	
1.2	How many weeks or months pregnant are you now? ఇప్పుడు మీరు ఎన్ని వారాల లేదా నెలల గర్భవతి?	Weeks ☐☐ OR Months ☐☐ Don't know..... -77	
1.3	How did you first learn or determine that you were pregnant? మీరు గర్భవతి అని ఎలా తెలుసుకున్నారు ? **[Prompt: The answer may be option B if the participant confirmed her pregnancy with the pregnancy kit you just completed in the field]**	Missed period ..... A Confirmation by urine or blood test by health professional ..... B Pregnancy symptoms such as nausea, breast tenderness and/or increase in appetite ..... C Confirmation by ultrasound by health professional..... D Other _____ E	
1.4	Do you plan to move to a different home, for instance your parents' home, during your pregnancy? మీరు ఈ గర్భంతో ఉన్నప్పుడు వేరే ఇంటికి వెళ్లాలని, తల్లిగారి ఇంటికి వెళ్లాలని ఏమైన అనుకుంటున్నారా?	Yes.....1 No.....0 Don't know..... ...77 Did not answer.....88	2.1
1.5	During which month of your pregnancy will you go to this other home? గర్భంతో ఉన్నప్పుడు మీరు ఏ నెలలో వేరే ఇంటికి వెళతారు?	Month of pregnancy ☐☐ Don't know/depends on husband or parents.....77	
1.6	How long do you intend to stay at this home? ఈ ఇంట్లో మీరు ఎంతకాలం ఉండాలనుకుంటున్నారు ?	How many months total ☐☐ OR Until how many months after delivery ☐☐ Don't know/depends on parents..... ... -77	
1.7	Can we contact you by telephone at the place you are moving? మీరు వెళ్తున్న ప్రదేశంలో మేము ఫోన్ ద్వారా మిమ్మల్ని సంప్రదించవచ్చా?	Yes.....1 No.....0 Don't know..... ...77 Did not answer.....88	2.1

1.8	What is the telephone number? మీ యొక్క టెలిఫోన్ నంబర్ ఏమిటి?	|_____| ENTER TELEPHONE NUMBER Don't know……..... …77	
1.9	Whose telephone is it? ఈ టెలిఫోన్ ఎవరిది?	Parents …….. 1 Grandparents …… 2 Sibling ……... 3 Other family member _____ 4 specify Friends …….. 5 Someone else _____ 6 specify	
2. HEALTH **Next, I have some general questions about your health and your health history**			
2.1	Would you say your health in general is very good, good, average or poor? సాధారణంగా మీ ఆరోగ్యం ఎలా ఉందను కుంటున్నారు ? చాలా బాగుందా, బాగుందా, మామూలుగా ఉందా లేక బాగా లేదా?	Very good ……1 Good ……....2 Average……..3 Poor……..4	
2.2	Have you **ever in your life** had any of the following? మీ జీవితకాలంలో మీరు ఎప్పుడైనా ఈ క్రింది వాటిలో దేనితోనైనా బాధపడ్డారా?	YES NO DON'T KNOW	
	a. Itching or irritation over the vulva యోని దగ్గర దురద మరియు చిరాకు	1 0 77	
	b. Vaginal pain యోని నొప్పి	1 0 77	
	c. Pain during urination మూత్రం వెళ్లినపుడు నొప్పి	1 0 77	
	d. Swelling in the groin గజ్జం దగ్గర వాపు	1 0 77	
	e. Pain in the lower abdomen not related to menses నెలసరికి సంబంధం లేకుండ పొత్తి కడుపులో నొప్పి	1 0 77	
	f. Bleeding between menstrual periods (not caused by Sunday/Monday pills) నెలసరికి మధ్యలో రక్తస్రావం (ఎర్రబట్ట) కలగడం (ఆదివారం/సోమవారం మాత్రల వల్ల కాకుండ)	1 0 77	
	g. Abnormal vaginal odor యోని వద్ద అసాధారణమైన వాసన	1 0 77	
	h. Pain during sexual intercourse దాంపత్యంలో కలిసినప్పుడు నొప్పి కలగడం	1 0 77	
	i. Spotting after sexual intercourse దాంపత్యంలో కలిసినప్పుడు రక్తం చుక్కలు కారడం	1 0 77	

2.3	Have you **ever in your life** experienced abnormal vaginal discharge? మీకు ఎప్పుడైనా యోని నుండి అసాధారణమైన స్రావం (తెల్లబట్ట) కలిగినదా ? **[Prompt: Abnormal vaginal discharge may have an unusual color, texture or odor. It is "abnormal" if they have more discharge than usual]**	Yes.....1 No.....0 Don't know.....77 Did not answer.....88	→ 3.1
2.4	What was the texture of the discharge? ఆ తెల్లబట్ట సాంద్రత ఎలా ఉండినది ?	Sticky mucoid.....A Frothy.....B Curdish.....C Pus like.....D Same as usual.....E Don't know.....77 Did not answer.....88	
2.5	What was the odour of the discharge? ఈ స్రావం వాసన ఎలా ఉండినది ?	Foul.....A Same as usual.....B Don't know.....77 Did not answer.....88	
2.6	What color was the discharge? ఈ స్రావం ఏ రంగులో ఉండినది ?	White/gray.....A Colourless.....B Yellow/green.....C Brown.....D Bloody.....E Don't know.....77 Did not answer.....88	
2.7	Has there ever been a time when you experienced lower abdominal pain and at least one or more of the following symptoms together? మీకు ఎప్పుడైన పొత్తి కడుపులో నొప్పి మరియు ఈ క్రింద ఉన్నటు వంటి లక్షణాలలో కనీసం ఒకటి లేక ఎక్కువ లక్షణాలు ఒకేసారి కలిగాయా? 1. Fever జ్వరం 2. vaginal bleeding not related to menses వెలసరికి సంబంధం లేకుండ రక్తస్రావం (ఎర్రబట్ట) కలగడం 3. Abnormal vaginal discharge యోని వద్ద అసాధారణమైన స్రావం 4. pain during urination? మూత్రం వెళ్లినప్పుడు నొప్పి	Yes.....1 No.....0 Don't know.....77 Did not answer.....88	3.1

2.8	How many times have you experienced this set of symptoms? మీరు ఎన్నిసార్లు ఈ విధమైన లక్షణాలను అనుభవించారు ?	Times ☐☐	
2.9	Are you currently experiencing lower abdominal pain and at least one of the following other symptons : fever, vaginal bleeding, abnormal vaginal discharge and/or pain during urination ? మీరు పొత్తి కడుపులో నొప్పి మరియు ఈ క్రింది వాటిలో కనీసం ఏ ఒక్క దైనా ప్రస్తుతం అనుభవిస్తున్నారా? లక్షణాలుః జ్వరం, యోనిస్రావము, అసాధారణమైన యోనిస్రావము మరియు మూత్రం వెళ్ళినప్పుడు నొప్పి	Yes.....1 No.....0 Did not answer.....88	
2.10	Did you receive medical treatment when you were experiencing all of these symptoms? మీరు ఈ లక్షణాలన్నింటిని అనుభవించేటప్పుడు మీరేమైన వైద్యం తీనుకున్నారా ?	Yes.....1 No.....0 Don't know.....77 Did not answer.....88	→ 3.1
2.11	Where did you go for treatment of these symptoms? ఈ లక్షణాల కొరకు మీరు ఎక్కడ చికిత్స చేయించుకున్నారు ?	UHC/UHP/UFHC/CHC/PHC/SC (Public Hospital) ..... A Private Clinic or Doctor's Office .....B Registered Medical Practitioner (RMP)/ Homeopath .....C MediCiti .....D Private Nursing Home or Private Hospital – other than MediCiti ..... E Traditional Healer ..... F Some Other Place _____ G Specify Don't know/unknown ..... 77 Did not answer question 88	
2.12	What kind of medical treatment did you have to treat these symptoms? ఈ లక్షణాల చికిత్సకై మీరు ఏ విధమైన వైద్యం తీనుకున్నారు ?	Did not get any treatment.....A Received pills.....B Received an injection .....C Got intravenous medicine in the hospital (inpatient).....D Other _____ E (specify) Don't know.....77 Did not answer question 88	

3. CURRENT HEALTH STATUS

3.1	Have you had any of the following **during the past 30 Days?** గడచిన 30 రోజుల్లో ఈ క్రింది వాటిలో దేనితోనైనా బాధపడ్డారా ?	YES NO NO. OF DAYS ILL	
	a. Diarrhea విరేచనాలు	1 0 ☐☐	
	b. Blood in stools మలంలో రక్తం	1 0 ☐☐	
	c. Respiratory infections (cough etc) శ్వాసకోస వ్యాధులు (దగ్గు మొదలైనవి)	1 0 ☐☐	
	d. Throat infections (sore throat) గొంతు వ్యాధులు	1 0 ☐☐	
	e. Urinary tract infection మూత్ర సంబంధిత వ్యాధి **[prompt: burning, blood in urine, difficulty starting or stopping urination]**	1 0 ☐☐	
	f. Fever జ్వరం	1 0 ☐☐	
	g. Mental stress, depression, problems with emotions మానసిక ఒత్తిడి, క్రుంగిపోవుట భావోద్రేక సమస్యలు	1 0 ☐☐	
3.2	**In the past 30 days**, did you take any antibiotic or medication or pills or injection for any infection? గడచిన మాసంలో మీరు ఏదేని వ్యాధి కొరకు యాంటీ బయాటిక్ మందులు లేక సూదులు తీసుకున్నారా ?	Yes.....1 No.....0 Don't know.....77 Did not answer.....88	3.4
3.3	*Interviewer should first write down any medications to be coded later as antibiotics* ఇంటర్వ్యూ చేయువారు మందు పేరు ఒక ప్రక్కన వ్రాసుకోవాలి తరువాత అవి యాంటీబయాటిక్ మందులో కాదో కోడ్ చేసుకోవాలి.	Days Taken ☐☐ Medications (specify) 1 _____ 2 _____ 3 _____ 4 _____	
3.4	**In the past 30 days**, were there any days that you were not able to do your regular duties because of illness or injury? గడచిన మాసంలో అనారోగ్యం/గాయం వల్ల మీరు మామూలుగా చేయు పనులు చేయలేకపోయారా ?	Yes.....1 No.....0 →	3.6

3.5	How many days were you unable to do your regular duties because of injury/ illness? ఎన్ని రోజులు అనారోగ్యం / గాయం వల్ల రోజూ చేయు పనులు చేయలేకపోయారు ?	Injury ☐☐ Days Illness ☐☐ Days	
3.6	**In this question I am asking about vitamin deficiencies. When someone is missing certain vitamins in their diets there are three things they might experience:** **very sore and swollen tongue;** **cracks and soreness at the corners of the mouth;** **night blindness.** **These symptoms of vitamin deficiency would last a long time, difficult to treat, and would probably get worse over time before getting better.** **ఈ ప్రశ్నలో నేను విటమిన్ల లోపాలను గురించి అడుగుతాను. కొంతమందికి ఆహారములో విటమిన్లు లోపించినట్లయితే** వారికి నాలుకపై పుండ్లు, పొక్కులు, నోటి చివర పగుళ్ళు, రేచీకటి లాంటి లక్షణాలు కలుగవచ్చును. ఈ లక్షణాలు విటమిన్ల **లోపమునకు కారణము, ఇవి చాలా కాలం ఉంటాయి మరియు చికిత్స చేయుటకు చాలా కష్టము.**		
	Since you became pregnant, have you had sore tongue, cracks at the corners of the mouth, night blindness that lasted more than a week and got worse over time? మీరు గర్భవతిగా ఉన్నప్పుడు మీరు వారం కంటే ఎక్కువ కాలం ఎప్పుడైనా నాలుకపై పుండ్లు, పొక్కులు లేక రేచీకటిలాంటి లక్షణాలను అనుభవించారా ?	YES NO MEDICATION a. Sore tongue నాలుకపై పుండు — 1 0 [_____] b. Cracks at the corners of the mouth నోటి చివరిలో పగుళ్ళు మరియు పొక్కులు — 1 0 [_____] c. Night blindness రేచీకటి — 1 0 [_____]	
4. HEALTH DURING YOUR CURRENT PREGNANCY			
4.1	Have you had any vaginal bleeding since your last menstrual period? గత నెలసరి తరువాత మీకు (మధ్యలో) రక్తస్రావం ఏమైనా జరిగిసదా ?	Yes……1 No……0 Don't know……77 Did not answer……88	→ 4.3
4.2	How many pads/cloths did you use for the bleeding at its heaviest in a day? మీకు రక్తస్రావం (ఎర్రబట్ట) ఎక్కువగా అయిసప్పుడు మీరు రోజుకి ఎన్ని ప్యాడ్‌లు/బట్టలు వాడారు ?	Spotting …… 1 1-2 pads per day…… 2 3-4 pads per day ……3 >4 pads per day …… 4 1-2 cloths per day …… 5 3-4 cloths per day …… 6 >4 cloths per day …… 7 Don't know……77 Did not answer…… 88	

4.3	Have you been experiencing nausea and/or vomiting? మీకు ఎప్పుడైనా తల తిరగడం లేక వాంతులు అవ్వడం జరిగిసదా ?	Yes……..……1 No……..……0 Don't know……..…… ……77 Did not answer……...88	5.1
4.4	For how many weeks during this pregnancy did you experience nausea/vomiting? మీరు ఈ గర్భంతో ఉన్నప్పుడు ఎన్ని వారాలు మీకు తల తిరగడం లేక వాంతులు అవ్వడం జరిగింది?	Weeks ☐☐	
4.5	How many days in a week do you experience nausea/vomiting? వారంలో ఎన్ని రోజులు మీకు తల తిరగడం/ వాంతులు అవ్వడం జరిగింది?	Days ☐	
4.6	What time of day do you experience nausea/vomiting occur? దినంలో మీకు ఏ సమయంలో తల తిరగడం/ వాంతులు అవ్వడం జరుగుతుంది?	Morning ……..…… A Afternoon ……..…… B Evening ……..…… C All times of day ……..……D	

5. ANTENATAL CARE

I would like to ask you some questions about your current pregnancy.
నేను ఈ గర్భం గురించి కొన్ని ప్రశ్నలు అడుగుతాను

Investigator Reads to Participant: Ante-Natal Care, or ANC visits are visits with a trained health care professional aimed at preparation of the pregnant woman for birth and management of complications, if any, during her pregnancy. Some goals of ANC visits are health and nutrition promotion and detection of high risk pregnancy.
ఇంటర్వ్యూ చేసేవారు పాత్రదారికి చదివి వినిపించాలి:
తర్ఫీదైన ఆరోగ్య కార్యకర్తచే జరుపబడిన ఎఎన్‌సి లేక ఎఎన్‌సి విజిట్స్/చెకప్ యొక్క ఉద్ధేశ్యమేమనగా స్త్రీ గర్భవతిగా సున్నప్పుడు ఒకవేళ ఏమైనా జబ్బు చేసినచో తనని తాను ఎలా రక్షించుకోవాలి మరియు కాన్పుకి ఎలా సిద్ధముగా ఉండాలి అని తెలియచేయడం. మరికొన్ని ఎఎన్‌సి విజిట్స్ హైరిస్క్ బిడ్డ పుట్టకుండా ఉండేందుకు ఆరోగ్య మరియు ఆహార ప్రాధాన్యతలను పరిశీలించబడును.

5.1	During this pregnancy, have you had your first ANC visit with a health care professional? ఇప్పుడున్న గర్భమునకు, మీరు మొదటి ఎఎన్‌సి విజిట్ ఆరోగ్య కార్యకర్త ద్వారా చేయించుకున్నారా? **[Prompt: If this interview is being conducted during their first visit, at MediCiti, mark Yes.]** మెడిసిటిలో వారి మొదటి ఎఎన్‌సి జరుగుతు వుంటే ' అవును' అని గుర్తించండి.	Yes……..……1 No……..……0 Don't know……..…… ……77 Did not answer……...88	5.10
5.2	When did you have your first ANC visit/checkup for this pregnancy? ఇప్పుడున్న గర్భమునకు, మీరు మొదటి ఎఎన్‌సి విజిట్/ చెకప్‌గాని ఎప్పుడు చేయించుకున్నారు ? **[Prompt: If this interview is being conducted during their first visit, at MediCiti, put today's date]**	☐☐ Day ☐☐ Month ☐☐☐☐ Year Don't know……..... -77 Don't know Day…….. -78 Don't know Month…… -79	

5.3	Where have you had ANC visits? మీరు ఎఎన్‌సి చెకప్‌లు ఎక్కడ చేయించుకున్నారు ? **[Prompt: Please list all health care facilities where participant has had ANC visits]**	UHC/UHP/UFHC/CHC/PHC/SC (Public Hospital) … ……..…….....A MediCiti Hospital ……..B Private Health Facility (Clinic, Doctor's Office, Nursing Home or Hospital) ……...C DAI (Traditional Birth Attendant) …….D Government Trained Birth Attendant ……E Some Other Place _____ F specify Don't know/unknown ……..……77 Did not answer question ……..88	
5.4	Who chose this health provider for your ANC? ఈ ఆరోగ్య కార్యకర్తను మీ ఎఎన్‌సి కొరకు ఎవరు ఎన్ని కచేసారు?	I did (woman) ……..……... A Mother-in-law / Father-in-law……... B Mother / Father …….. C Husband ……... D Health Functionary ……E Someone else _____ F (Specify) Don't know/unknown ……..…. 77 Did not answer question ……... 88	
5.5	Why was this health facility chosen? ఈ ఆరోగ్య కేంద్రమునే ఎందుకు ఎంచుకున్నారు ? **[Prompt: If the woman did not choose the health facility and does not know why it was chosen, mark Don't know, 77]**	Proximity/closeness to house …….. A I/my family have received care there before …….. B Recommended by friend or family member …….. C Quality of care is good …….. D Services are more affordable than other places. ……..…. E It is the only place near enough …..……..…. F Other reason _____ G specify Don't know/unknown ……77 Did not answer question ……..88	
5.6	How many ANC visits, during the current pregnancy, have you had including today? మీరు ప్రస్తుతం గర్భవతిగా ఉన్నందున ఈ రోజుతో కలిపి ఎన్ని ఎఎన్‌సి చెకప్‌లు చేయించుకున్నారు ?	Visits ☐☐	
5.7	Has your <u>health care provider</u> given you an expected date of delivery for this pregnancy? మీ ఆరోగ్య సంరక్షణ చేసే డాక్టర్ మీరు ప్రసవించే తేది చెప్పినారా ?	Yes……1 No……0 Don't know…….....…..…77 Did not answer……...88	→ 5.14

5.8	What is your expected date of delivery? మీరు ప్రసవించే తేది ఏమి ?	☐☐ ☐☐ ☐☐☐☐ Day Month Year Don't know..... -77 Don't know Day..... -78 Don't know Month..... -79	
5.9	How did the health care provider determine the expected date of delivery? మీరు ప్రసవించే తేదిని డాక్టర్ ఎలా నిర్ధారించారు ?	By dates, using my last menstrual period ..... A By ultrasound ..... B Other method _____ G specify Don't know/unknown ..... 77 Did not answer question 88	5.14
5.10	Do you plan on eventually going for/receiving ANC from a health professional? చివరి వరకు మీరు ఆరోగ్య కార్యకర్త వద్దకు ఎఎన్‌సి కొరకు వెళ్లాలని నిర్ణయించుకున్నారా?	Yes.....1 No.....0 Don't know..... .....77 Did not answer.....88	5.14
5.11	Where will you go for ANC? ఎఎన్‌సి కొరకు మీరు ఎక్కడికి వెళతారు?	UHC/UHP/UFHC/CHC/PHC/SC (Public Hospital) ..... A Private Clinic or Doctor's Office ..... B MediCiti ..... C Private Nursing Home or Private Hospital – other than MediCiti ..... D DAI (Traditional Birth Attendant) ..... E Some Other Place _____ F specify Don't know/unknown ....77 Did not answer question 88	
5.12	Who will decide when is the right time to start receiving ANC services? ఎఎన్‌సి సేవలు స్వీకరించుటకు ఇది సరి అయిన సమయమని ఎవరు నిర్ణయిస్తారు ?	I will (woman) ..... A Mother-in-law / Father-in-law..... B Mother / Father ..... C Husband ..... D Health Functionary ..... E Someone else _____ F specify Don't know/unknown ..... 77 Did not answer question 88	
5.13	When will you go to receive ANC services from a health care provider? ఎఎన్‌సి సేవలు తీసుకొసుటకు మీరు ఆరోగ్య కార్యకర్త వద్దకు ఏ రోజున వెళతారు ? **[Prompt: Investigator, take note of this date so that LIFE Staff can meet the woman if she comes to MediCiti for her ANC visit]**	☐☐ ☐☐ ☐☐☐☐ Day Month Year OR Month of pregnancy ..... ☐☐ Don't know/unknown ..... -77	

5.14	Do you know where you will deliver your baby? మీ బిడ్డను ఎక్కడ ప్రసవిస్తారో మీకు తెలుసా ?	Yes……1 No……0 Don't know…….....…77 Did not answer……...88	5.16
5.15	Where will you deliver your baby? మీరు మీ బిడ్డను ఎక్కడ ప్రసవిస్తారు ?	UHC/UHP/UFHC/CHC/PHC/SC (Public Hospital) ……..... A MediCiti …… B Private Nursing Home or Private Hospital – other than MediCiti …….. C At home with Birth Attendant…….. D At home without Birth Attendant…….. E Some Other Place _____ F specify Don't know…….. 77 Did not answer question …… 88	
5.16	Have you had any pregnancy related visit with a health professional that was **not** an ANC visit? మీరు ఎఎన్‌సి విజిట్ కాకుండ ఇంక ఏవైన గర్భాధారణకు సంబంధించి ఆరోగ్య కార్యకర్తని కాని/ డాక్టర్‌ని కాని సంప్రదించారా?	Yes……1 No……0 Don't know…….....…77 Did not answer……...88 **Check if 5.1 in 'No' and also 5.16 is 'No'**…… ☐	5.19 6.1
5.17	How many of these non-ANC visits have you had? ఎఎన్‌సి సందర్శన కాకుండ ఎన్నిసార్లు సంప్రదించారు?	Visits ☐☐	
5.18	With whom did you have this non-ANC visit? మీరు ఎవరిని సంప్రదించారు ?	UHC/UHP/UFHC/CHC/PHC/SC (Public Hospital) … ……..... A MediCiti Hospital …… B Private Health Facility (Clinic, Doctor's Office, Nursing Home or Hospital) …… C DAI (Traditional Birth Attendant) …… D Government Trained Birth Attendant ……E Some Other Place _____ F specify Don't know/unknown …… 77 Did not answer question …….. 88	

5.19	**During your current pregnancy** have you **been told by a doctor or other health care provider** that you had any of the following conditions? ప్రస్తుతం ఈ గర్భం దాల్చిన తరువాత మీకు డాక్టర్ లేక ఆరోగ్య సంరక్షకులు ఈ క్రింది వాటిలో ఏమైనా ఉన్నాయని చెప్పినారా ?				
		YES	NO	DON'T KNOW	
	a. Sugar Disease షుగర్ వ్యాధి	1	0	77	
	b. High Blood Pressure అధిక రక్తపోటు	1	0	77	
	c. Swelling of your feet పాదాల వాపు	1	0	77	
	d. Swelling of your face ముఖం వాపు	1	0	77	
	e. Contractions of your uterus గర్భకోశంలో కాంట్రాక్షన్స్ రావడం	1	0	77	
	f. Very sore throat for several days or more చాలా రోజులుగా గొంతు నొప్పి	1	0	77	
	g. Anemia రక్తహీనత	1	0	77	
	h. One or more sores on your genitals యోని వద్ద ఒకటి లేక ఎక్కువ కురుపులు	1	0	77	
	i. A vaginal discharge యోనిస్రావము	1	0	77	
	j. Diarrhea నీళ్ళ విరేచనాలు	1	0	77	
	k. Jaundice పసికర్లు	1	0	77	
	l. Burning or pain when you urinate మూత్రం పోసేటప్పుడు నొప్పి లేక మంట	1	0	77	
	m. Goiter గొంతులో కణితి	1	0	77	
	n. Any other pregnancy related condition ఇంక ఏదైన గర్భాధారణకి సంబంధించిన బాధ _____ specify	1	0	77	

6. Vitamins			
6.1	Since you first suspected that you were pregnant, have you taken any multi vitamins or prenatal vitamins? మీరు గర్భవతి అని తెలిసినప్పటి నుండి మీరు ఏమైనా విటమిన్ బిళ్ళలు తీసుకున్నారా ? **(PROMPT: with names of local multi-vitamins or prenatal vitamins)**	Yes.....1 No.....0 Don't know..... ...77 Did not answer.....88	**7.1**
6.2	Did you receive vitamins/tablets at your first ANC visit? మీరు మీ మొదటి ఎఎన్‌సి చెకప్ అప్పుడు విటమిన్లు/ బిళ్లలు స్వీకరించారా ? **[PROMPT: Ask to look at any tablets received at first ANC visit. Assume that any tablets not for a specific illness or infection are vitamins]**	Yes.....1 No.....0 Has not completed first ANC .....2 Don't know..... ...77 Did not answer.....88	
6.3	Did you receive Iron-Folic-Acid (IFA) tablets from the Primary Health Center? మీరు ఆరోగ్య కేంద్రము నుండి ఐరన్ ఫోలిక్ యాసిడ్ బిళ్లలు స్వీకరించారా ? **[Prompt: Show blister pack with IFA tablets as an example]**	Yes.....1 No.....0 Don't know..... ...77 Did not answer.....88	
6.4	What are the vitamins you are taking? మీరు ఏయే విటమిన్ బిళ్ళలు తీసుకుంటున్నారు ? **[PROMPT: Ask to see bottle and record the name of the vitamins.]**	Vitamin C ..... A Vitamin A ..... B Vitamin B12 ..... C Calcium ..... D Vitamin D ..... E Vitamin E ..... F Folic Acid ..... G IFA Tablets ..... H Other _____ I Specify Don't know..... 77	
6.5	When did you start taking the vitamins/tablets? మీరు విటమిన్ బిళ్లలు వేసుకోవడం ఎప్పటి నుండి మొదలు పెట్టారు ?	☐☐ ☐☐☐☐ Month Year OR Month of Pregnancy ..... ☐☐ Don't know..... -77	

6.6	When you first got them, how often did you take the vitamins/tablets? మీరు విటమిన్ బిళ్లలు ఎప్పుడు తెచ్చుకున్నారు, ఎంత తరచుగా వేసుకున్నారు ?	1 each day .....1 2 each day .....2 3 or more each day ..... 3 1-3 each week ..... 4 4-6 each week .....5 Only a few days a month..... 6 Other _____ 7 Describe Don't know..... ...77 Did not answer.....88	
6.7	Since then **(prompt: date given above),** did you change how often you were taking the vitamins/tablets? మీరు విటమిన్లు తీసుకోవడం మొదలు పెట్టినప్పటి నుండి ఎంత తరచుగా మీ క్రమమును మార్చి వేసారు ?	No change ..... 1 → 6.10 Stopped for >1 week ..... 2 Took more vitamins ..... 3 Took fever vitamins ..... 4 Don't know..... ...77 Did not answer.....88	6.10
6.8	Did you stop because you were experiencing nausea or vomiting? మీకు కడుపులో తిప్పడం లేక వాంతి కలగడం వలన ఆపు చేసారా ?	Yes.....1 → 6.10 No.....0 Don't know..... ...77 Did not answer.....88	
6.9	Why did you stop taking the vitamins? మీరు విటమిన్ బిళ్లలు వేసుకోవడం ఎందుకు మాని వేసారు ?	Describe: _____ _____	
6.10	In the **last seven days,** how many days did you take a prenatal or multi vitamin? గడచిన వారములో ఎన్ని రోజులు మీరు విటమిన్ బిళ్లలు తీసుకున్నారు ?	Every day ..... 1 6 days ..... 2 5 days ..... 3 4 days ..... 4 3 days ..... 5 2 days ..... 6 1 day ..... 7 Did not take any day..... 8	

7. PREGNANCY HISTORY

<u>These next questions are about any pregnancies you may have had in the past including current pregnancy</u>

7.1	Did you have any problem conceiving with any of your pregnancies? Was their any delay in conceiving, in your opinion? మీరు గర్భవతి అయిన ప్రతిసారి ఏమైనా ఇబ్బందులు కలిగేనా ? అసగా గర్భవతి కావడానికి మీ ఉద్దేశ్యం ప్ర కారం ఏమైనా ఆలస్యం జరిగిసదా ?	Yes.....1 No.....0 Don't know..... ...77 Did not answer.....88	→7.4
7.2	Have you or your husband ever talked about fertility problems with a doctor? మీరు గాని లేక మీ భర్తగాని ఎప్పుడైనా పిల్లలు కలగడానికి సంబంధించిన విషయమై డాక్టర్‌తో మాట్లాడినారా ?	Yes.....1 No.....0 Don't know..... ...77 Did not answer.....88	7.4

7.3	Did the doctor tell you that you had any of the following infertility problems? మీ డాక్టర్ మీకు పిల్లలు కలుగకపోయే అవకాశమున్నదని చెప్పినారా ?	Problems with ovulation……A Problems with menstruation …….. B Blocked tubes……C Other tube or pelvic problems……D Endometriosis……E Semen or sperm problems..……F Any other infertility problems……G Other_____ H (specify) Don't know……77 Did not answer…….. 88	
7.4	Have you ever been pregnant before this pregnancy? ఈ గర్భముసకు ముందు మీరు ఎప్పుడైనా గర్భవతిగా ఉన్నారా ? Please include live births, miscarriages, stillbirths, ectopic pregnancies, abortions and pregnancy terminations.	Yes……1 No……0 Don't know……..... …77 Did not answer……...88	8.1
7.5	How many times have you been pregnant before this pregnancy (include live births, miscarriages, stillbirths, ectopic pregnancies, abortions and pregnancy terminations)? మీరు ఈ గర్భము దాల్చక ముందు ఎన్నిసార్లు గర్భవతి అయ్యారు ?	Pregnancies ☐☐	
7.6	How old were you when you became pregnant for the **first** time? మీరు మొదటిసారి గర్భవతి అయినప్పుడు మీ వయస్సెంత ?	Age ☐☐	

7.7	During your **previous {pregnancy/pregnancies}** <u>were you told by a doctor or other health care provider</u> that you had any of the following conditions? ఇది వరకు మీరు గర్భవతిగా ఉన్నప్పుడు మీకు డాక్టర్ లేక ఆరోగ్య సంరక్షకులు ఈ క్రింది వాటిలో ఏమైనా ఉన్నాయని చెప్పినారా ?	YES	NO	DON'T KNOW
	a. Sugar Disease షుగర్ వ్యాధి	1	0	77
	b. High Blood Pressure అధిక రక్తపోటు	1	0	77
	c. Preeclampsia మూర్ఛ వ్యాధి	1	0	77
	[Prompt: High BP & protein in urine]			
	d. Swelling of your feet గర్భవతిగా ఉన్నపుడు కాళ్ళవాపు	1	0	77
	e. Swelling of your face ముఖం వాపు	1	0	77
	f. Early contractions of your uterus గర్భకోశంలో కాంట్రాక్షన్స్ రావడం	1	0	77
	g. Very sore throat for several days or more చాలా రోజులుగా గొంతు నొప్పి	1	0	77
	h. Anemia రక్తహీనత	1	0	77
	i. One or more sores on your genitals యోని వద్ద ఒకటి లేక ఎక్కువ కురుపులు	1	0	77
	j. Abnormal vaginal discharge అసాధారణమైన యోని స్రావము	1	0	77
	k. Jaundice పసికర్లు	1	0	77
	l. Burning or pain when you urinate మూత్రం పోసేటప్పుడు మంట లేక నొప్పి	1	0	77
	m. Diarrhea నీళ్ళ విరేచనాలు	1	0	77
	n. Goiter గొంతులో కణితి	1	0	77
	o. Any other pregnancy related condition ఇంక ఏదైనా గర్భాధారణకి సంబంధించిన బాధ	1	0	77
	_____ Specify	1	0	77

<u>Now I'm going to ask about {each of} your {pregnancies/pregnancy}, {beginning with the first one.}</u>

		PREG #1	PREG #2	PREG #3	
7.8	In what month and year did your [FIRST/NEXT] pregnancy end? Or, what month and year was your baby born? ఏ నెల మరియు ఏ సంవత్సరములో మీ (మొదటి/తరువాత) బిడ్డ పుట్టినారు ?	☐☐ Day ☐☐ Month ☐☐☐☐ Year	☐☐ Day ☐☐ Month ☐☐☐☐ Year	☐☐ Day ☐☐ Month ☐☐☐☐ Year	

7.9	What was the outcome of this pregnancy? ఈ గర్భము ద్వారా కలిగిన ఫలితము ఏమి ?	Stillbirth …… 2 Miscarriage ... 3 Induced abortion …… 4 Tubal, ectopic pregnancy…. 5 Molar pregnancy ..... 6 Live birth ….. 1 7.11 ↵	Stillbirth …… 2 Miscarriage ... 3 Induced abortion …… 4 Tubal, ectopic pregnancy…. 5 Molar pregnancy ..... 6 Live birth ….. 1 7.11 ↵	Stillbirth …… 2 Miscarriage ... 3 Induced abortion …… 4 Tubal, ectopic pregnancy…. 5 Molar pregnancy ..... 6 Live birth ….. 1 7.11 ↵	
7.10	How many months pregnant were you when this pregnancy ended? ఈ గర్భము పూర్తి అయ్యే నాటికి మీరు ఎన్ని నెలల గర్భవతి? **[probe: try to find out weeks, if woman is unclear, record based on knowledge of months pregnant]**	☐☐ Months	☐☐ Months	☐☐ Months	
7.11	Did you receive antenatal care during this pregnancy? ప్రస్తుతం గర్భవతి అయిన తర్వాత ఎఎన్‌సి చెకప్ చేయించుకున్నారా ?	Yes …… 1 No …….. 0 7.13 ↵	Yes …… 1 No …….. 0 7.13 ↵	Yes …… 1 No …….. 0 7.13 ↵	
7.12	If yes, how many ANC visits did you have during the pregnancy? ఒకవేళ అవును అయితే ప్రస్తుతం గర్భవతి అయిన తరువాత ఎన్నిసార్లు ఎఎన్‌సి చెకప్‌లు చేయించుకున్నారు ?	☐☐ Visits <3 …… 1 >3 …… 2 Don't Know 77	☐☐ Visits <3 …… 1 >3 …… 2 Don't Know 77	☐☐ Visits <3 …… 1 >3 …… 2 Don't Know 77	
7.13	During this pregnancy, were you diagnosed with preeclampsia? ప్రస్తుతం గర్భవతి అయిన తరువాత మీకు మూర్ఛ వ్యాధి కలదని నిర్ధారణ చేసినారా ? **[Prompt: High blood pressure and protein in the urine]**	Yes ……... 1 No ……0 Don't Know 77	Yes ……... 1 No ……0 Don't Know 77	Yes ……... 1 No ……0 Don't Know 77	
7.14	During this pregnancy, were you diagnosed with diabetes? ప్రస్తుతం గర్భవతి అయిన తరువాత మీకు షుగర్‌వ్యాధి ఉన్నదని నిర్ధారణ చేసినారా ? **[Prompt: sugar disease during pregnancy when you didn't have sugar disease before pregnancy]**	Yes ……... 1 No ……0 Don't Know 77	Yes ……... 1 No ……0 Don't Know 77	Yes ……... 1 No ……0 Don't Know 77	

IF NOT LIVEBIRTH, GO BACK TO QUESTION 7.8 IN THE NEXT COLUMN IF NO MORE PREGNANCIES, GO TO QUESTION 8.1					
7.15	How many babies did you give birth to? మీరు ఎంతమంది పిల్లలను కన్నారు?	Single birth ... 1 Twins …….. 2 →	Single birth ... 1 Twins …….. 2 →	Single birth ... 1 Twins …….. 2 →	If twins → 7.25
		Triplets …… 3 Other _____ 4 specify	Triplets …… 3 Other _____ 4 specify	Triplets …… 3 Other _____ 4 specify	
7.16	Was the baby a boy or girl? ఆ బిడ్డ పాప లేక బాబా ?	Boy ……. 1 Girl ……. 2	Boy ……. 1 Girl ……. 2	Boy ……. 1 Girl ……. 2	
7.17	What was the birth weight? పుట్టినప్పుడు బరువెంత ? **Please indicate if this is the mother's memory of birth weight or ask if she has the child's medical card with birth weight <u>written</u> on it.**	☐.☐☐☐ KG Don't Know -77 No answer -88 Memory …… 1 Medical card .. 2	☐.☐☐☐ KG Don't Know -77 No answer - 88 Memory …… 1 Medical card .. 2	☐.☐☐☐ KG Don't Know -77 No answer -88 Memory …… 1 Medical card ..2	
7.18	Was the baby born **before** the expected delivery date? మీరు ప్రసవించవలసిన తేది కన్నా ముందే ప్రసవించారా ? How many weeks or days early? ఎన్ని రోజులు లేక వారాల ముందు ?	Yes …… 1 No ……. 0 ☐☐ Weeks early ☐☐ Days early	Yes …… 1 No ……. 0 ☐☐ Weeks early ☐☐ Days early	Yes …… 1 No ……. 0 ☐☐ Weeks early ☐☐ Days early	
7.19	Where was this baby born? ఈ బిడ్డ ఎక్కడ పుట్టినది ?	Public clin …. 1 Private clin … 2 Nurs Home .. 3 Matern Hom . 4 Public Hosp .. 5 MediCiti Hos. 6 Private Hosp.. 7 At home ….. 8 Other …….. 9 _____ specify	Public clin …. 1 Private clin … 2 Nurs Home .. 3 Matern Hom . 4 Public Hosp .. 5 MediCiti Hos. 6 Private Hosp.. 7 At home ….. 8 Other …….. 9 _____ specify	Public clin …. 1 Private clin … 2 Nurs Home .. 3 Matern Hom . 4 Public Hosp .. 5 MediCiti Hos. 6 Private Hosp.. 7 At home ….. 8 Other …….. 9 _____ specify	
7.20	Did the baby appear normal and healthy? బిడ్డ మామూలుగా మరియు ఆరోగ్యంగా ఉండేనా ? **[Prompt: Were there any physical birth defects]** [IF NO, DESCRIBE]	Yes …… 1 No ……. 0 Describe: _____ _____	Yes …… 1 No ……. 0 Describe: _____ _____	Yes …… 1 No ……. 0 Describe: _____ _____	

7.21	Did the baby have any serious illnesses at birth or within the first year of life? బిడ్డ పుట్టినప్పుడు లేక సంవత్సరం తిరిగే లోపల ఏమైనా తీవ్రంగా జబ్బు చేసిసదా ?	Yes ..... 1 No ..... 0 Describe: _____ _____ _____	Yes ..... 1 No ..... 0 Describe: _____ _____ _____	Yes ..... 1 No ..... 0 Describe: _____ _____ _____	
7.22	How is the child now? ప్రస్తుతం బిడ్డ ఎలా ఉన్నది ?	Alive ..... 1 → Dead 2	Alive ..... 1 → Dead 2	Alive ..... 1 → Dead 2	**If alive → 7.15** **If no more births → 7.39**
7.23	If the child died, what was wrong with the baby before he/she died? బిడ్డ చనిపోయి ఉంటే చనిపోయే నాటికి ముందు బిడ్డకు ఏమి కష్టముండిసది ?	_____ _____ _____	_____ _____ _____	_____ _____ _____	
7.24	How old was the baby when he/she died? బిడ్డ చనిపోయినప్పుడు పాప/బాబు వయస్సెంత?	Days ☐☐ Weeks ☐☐ Months ☐☐ Yr. ☐☐☐☐	Days ☐☐ Weeks ☐☐ Months ☐☐ Yr. ☐☐☐☐	Days ☐☐ Weeks ☐☐ Months ☐☐ Yr. ☐☐☐☐	
If baby was a single birth, go back to Question #7.15 in the 2nd column to ask about other pregnancies OR if this was the last pregnancy, skip to Question #7.39 For twin pregnancies, complete questions #7.25 – 7.38					
7.25	Was the first twin a boy or girl? కవలలలో మొదటి బిడ్డ ఆడ లేక మగా ?	Boy ..... 1 Girl 2	Boy ..... 1 Girl 2	Boy ..... 1 Girl 2	
7.26	What was the birth weight? పుట్టినప్పుడు బరువెంత ? **Please indicate if this is the mother's memory of birth weight or ask if she has the child's medical card with birth weight <u>written</u> on it.**	☐.☐☐☐ KG Don't Know -77 No answer -88 Memory ..... 1 Medical card .. 2	☐.☐☐☐ KG Don't Know -77 No answer -88 Memory ..... 1 Medical card .. 2	☐.☐☐☐ KG Don't Know -77 No answer -88 Memory ..... 1 Medical card . 2	
7.27	Was the first twin born **before** the expected delivery date? కవలలలో మొదటి బిడ్డ ప్రసవించే తేదీ కన్నా ముందే పుట్టినదా ? How many weeks or days early?	Yes ..... 1 No ..... 0 ☐☐ Weeks early ☐☐ Days early	Yes ..... 1 No ..... 0 ☐☐ Weeks early ☐☐ Days early	Yes ..... 1 No ..... 0 ☐☐ Weeks early ☐☐ Days early	

7.28	Where was the first twin born? మొదటి బిడ్డ ఎక్కడ పుట్టినాడు ?	Public clin …. 1 Private clin … 2 Nurs Home .. 3 Matern Hom . 4 Public Hosp .. 5 MediCiti Hos. 6 Private Hosp.. 7 At home …... 8 Other …….. 9 _____ specify	Public clin …. 1 Private clin … 2 Nurs Home .. 3 Matern Hom . 4 Public Hosp .. 5 MediCiti Hos. 6 Private Hosp.. 7 At home …... 8 Other …….. 9 _____ specify	Public clin …. 1 Private clin … 2 Nurs Home .. 3 Matern Hom . 4 Public Hosp .. 5 MediCiti Hos. 6 Private Hosp.. 7 At home …... 8 Other …….. 9 _____ specify	
7.29	Did the first twin appear normal and healthy? మొదటి కవల బిడ్డ మామూలుగా మరియు ఆరోగ్యంగా ఉండేనా ? **[Prompt: Were there any physical birth defects]** [IF NO, DESCRIBE]	Yes …….. 1 No ……. 0 Describe: _____ _____	Yes …….. 1 No ……. 0 Describe: _____ _____	Yes …….. 1 No ……. 0 Describe: _____ _____	
7.30	Did the first twin have any serious illnesses at birth or within the first year of life? మొదటి బిడ్డ పుట్టినప్పుడు లేక సంవత్సరము తిరిగే లోపల ఏమైనా తీవ్రముగా జబ్బు చేసినదా ?	Yes …….. 1 No ……. 0 Describe: _____ _____ _____	Yes …….. 1 No ……. 0 Describe: _____ _____ _____	Yes …….. 1 No ……. 0 Describe: _____ _____ _____	
7.31	How is the child now? ఇప్పుడు బిడ్డ ఎలా ఉన్నాడు ?	Alive ……. 1 → Dead …….. 2	Alive ……. 1 → Dead …….. 2	Alive ……. 1 → Dead …….. 2	→7.34
7.32	If the child died, what was wrong with the baby before he/she died? ఒకవేళ బిడ్డ చనిపోయి ఉంటే చనిపోయే నాటికి ముందు బిడ్డకు ఏమి కష్టముండినది ?	_____ _____ _____	_____ _____ _____	_____ _____ _____	
7.33	How old was the first twin when he/she died? మొదటి కవల బిడ్డ చనిపోయినప్పుడు పాప/బాబు వయస్సెంత ?	☐☐ Months ☐☐ Weeks ☐☐ Days	☐☐ Months ☐☐ Weeks ☐☐ Days	☐☐ Months ☐☐ Weeks ☐☐ Days	
7.34	Was the second twin a boy or girl? రెండవ కవల బిడ్డ ఆడ లేక మగా ?	Boy ……. 1 Girl ……. 2	Boy ……. 1 Girl ……. 2	Boy ……. 1 Girl ……. 2	
7.35	What was the birth weight? పుట్టినప్పుడు బరువెంత ? **Please indicate if this is the mother's memory of birth weight or ask if she has the child's medical card with birth weight <u>written</u> on it.**	☐.☐☐☐ KG Don't Know -77 No answer -88 Memory …… 1 Medical card .. 2	☐.☐☐☐ KG Don't Know -77 No answer -88 Memory …… 1 Medical card .. 2	☐.☐☐☐ KG Don't Know -77 No answer -88 Memory …… 1 Medical card... 2	

7.36	Did the second twin appear normal and healthy? రెండవ కవల బిడ్డ మామూలుగా మరియు ఆరోగ్యంగా ఉండేనా ? **[Prompt: Were there any physical birth defects]** [IF NO, DESCRIBE]	Yes ..... 1 No ..... 0 Describe: _____ _____	Yes ..... 1 No ..... 0 Describe: _____ _____	Yes ..... 1 No ..... 0 Describe: _____ _____	
7.37	Did the second twin have any serious illnesses at birth or within the first year of life? రెండవ కవల బిడ్డ పుట్టినప్పుడు లేక సంవత్సరము తిరిగే లోపు ఏమైనా తీవ్రముగా జబ్బు చేసిసదా ?	Yes ..... 1 No ..... 0 Describe: _____ _____ _____	Yes ..... 1 No ..... 0 Describe: _____ _____ _____	Yes ..... 1 No ..... 0 Describe: _____ _____ _____	
7.38	How is the child now? ప్రస్తుతం బిడ్డ ఎలా ఉన్నది ?	Alive ..... 1 Dead ..... 2 **If more births.....7.8** **If no more.....7.39**	Alive ..... 1 Dead ..... 2 **If more births.....7.8** **If no more.....7.39**	Alive ..... 1 Dead ..... 2 **If more births.....7.8** **If no more.....7.39**	

Go to next pregnancy in table (return to Question #7.8), or if no further pregnancies, go to following question (#7.39)

Summary – Complete based on answers to previous questions in the table.

7.39	Total Number of previous pregnancies ఇంతకు ముందు వచ్చిన మొత్తము గర్భముల సంఖ్య	Pregnancies ☐☐	
7.40	Total Number of previous live births ఇంతకు ముందు పుట్టి ఉన్న మొత్తము పిల్లల సంఖ్య	Live Births ☐☐	
7.41	**IF PREVIOUS LIVE BIRTH, ASK:** Are you currently nursing a baby? మీరు ప్రస్తుతం మీ బిడ్డకు మీ పాలు ఇస్తున్నారా ?	Yes.....1 No.....0 Don't know..... ...77 Did not answer.....88	8.1
7.42	How old is the baby you are nursing? మీరు మీ పాలిచ్చే బిడ్డ వయస్సెంత ?	Weeks ☐☐	
7.43	How many times per day are you nursing the baby? రోజుకి ఎన్నిసార్లు మీరు బిడ్డకు మీ పాలు త్రాగిస్తున్నారు ?	Times per day ☐☐	

8. DEPRESSION

These next questions are about your state of mind and mental health. With these five questions we are trying to see if you experience any of the symptoms of depression. Answering "yes" to any of these questions does not mean that you are "depressed" as it is normal for most people to feel some symptoms of depression from time to time. People may become depressed because of triggers in their lives like stress at work or problems in their home life. They may also become depressed when there is no obvious reason and everything seems fine in their life. While it is perfectly normal to feel sad or down from time to time, we are interested in whether you have experienced any of these symptoms in such a way that they overwhelm you or disrupt your regular life. For example, if a family member dies, it is normal to feel sad. But, we would like to know if you feel that kind of sadness even without an event like a death in the family or if that sadness overwhelms you to such an extent that you cannot take care of yourself or your family.

తరువాత వచ్చే ప్రశ్నలు మీ మానసిక ఆరోగ్యం గూర్చి ఉంటాయి. ఈ 5 ప్రశ్నలతో మీరు మానసిక లక్షణాలు అనుభవించారా అని తెలుసుకుంటాం. ఈ ప్రశ్నలలో దేనికైనా "అవును" అని సమాధానం ఇస్తే మీరు కృంగిపోయిన స్థితిలో ఉన్నారని కాదు మరియు ఈ లక్షణాలు సర్వ సాధారణంగా ఏదో సమయాల్లో ఉంటాయి. ప్రజలు వారి జీవితంలోని ఒత్తిడి, పనిలో ఒత్తిడి, లేక కుటుంబంలో సమస్యల వల్ల కృంగుదలకు గురికావచ్చును. జీవితంలో అన్ని సౌఖ్యంగా జరుగుతున్నప్పుడు కూడా ఏ కారణం లేకుండానే కృంగుదలకు గురికావచ్చును. విషాదాలు లేక ఎగుడుదిగుడ్లు ఏదో సమయాల్లో ఖచ్చితంగా సర్వ సాధారణము. మీరు ఏ లక్షణాలు అనుభవించారో, ఏ లక్షణాలు మీ జీవితాన్ని కలతపరిచాయో అనేది మేము తెలుసుకోవాలని ఇష్టపడుచున్నాము. ఉదా : ఒక కుటుంబంలో సభ్యుడు చనిపోతే బాధపడడం అనేది సహజం కానీ మీరు అటువంటి బాధను మీ కుటుంబంలో ఎవరూ చనిపోకుండానే అనుభవిస్తున్నారా లేక అటువంటి బాధకు గురి అయి కనీసం మీ గురించి మరియు మీ కుటుంబం గురించి శ్రద్ధ తీసుకోలేకపోతున్నారా అనేది మేము తెలుసుకోవాలసు కుంటున్నాము.

8.1	Have you had a pervasively sad or down mood or feeling of hopelessness? మీరు కృంగిపోవడం అనే భావన లేక నిరాశ భావాలు కలిగి యున్నారా ? (***Probe: have you felt like things were never going to get better, that you would never be happy, that everything was going wrong and these feelings made it hard for you to function on a day to day basis?*** ప్రేరేపించు : మాకు పరిస్థితులు ఎప్పుడూ బాగుపడవు. నేను సంతోషంగా ఉండను, ప్రతీది తప్పు జరుగుతుంది అనే ఆలోచనలు మిమ్మల్ని ఎక్కువగా బాధపెట్టి రోజువారి పనులు చేసుకోవడం కష్టంగా ఉంటుందా?	Yes……1 No……0 Don't know……..... .77 Did not answer ……...88	
8.2	Do you get less pleasure from things that you used to enjoy? మీరు సంతోషించు సమయాన తక్కువ ఆనందం పొందానని అనిపించిందా ? ***(probe: have you found that things you used to like, such as watching television or spending time with friends are no longer fun for you?)*** మీరు ఇష్టముతో చేయు పనులు అనగా, టి.వి. చూడడం, స్నేహితులతో గడపడం మీకు సంతోషాన్ని ఇవ్వడం లేదా ?	Yes……1 No……0 Don't know……..... .77 Did not answer ……...88	

8.3	Have you lost weight without any specific attempt to lose weight? మీరు ఏమి ప్రయత్నం చేయకుండానే బరువు తగ్గారా ? (***Probe: Are your clothes fitting differently or has anyone commented that you look thinner than before?)*** మీ బట్టలు మీకు వదులుగా ఉన్నాయా లేక ఎవరైనా మీరు ముందుకన్నా సన్నగా కనబడుతున్నారని చెప్పారా ?	Yes……1 No……0 Don't know……..77 Did not answer ……..88	
8.4	Do you have difficulty getting sleep, or wake up during night, or wake before everyone else wakes up? మీకు నిద్రపోవడం కష్టంగా గానీ, మధ్య రాత్రిలో మెలకువ రావడం లేక అందరికంటే ముందే నిద్ర లేవడం వంటివి వున్నాయా ?	Yes……1 No……0 Don't know……..77 Did not answer ……..88	
8.5	Do you have suicidal ruminations? మీకు ఆత్మహత్య చేసుకోవాలనే ఆలోచనలు కలుగుతున్నాయా ? ***(Probe: Have you thought about or imagined ways by which you might take your own life)*** మీ జీవితాన్ని అంతం చేసుకోవాలని ఎప్పుడైనా అనిపించిందా ?	Yes……1 No……0 Don't know……..77 Did not answer ……..88	
9. PREGNANCY PRACTICES			
9.1	Have you stopped working, or changed your work schedule in any way related to your pregnancy? మీరు గర్భవతిగా ఉండడం వలన బయట మరియు ఇంట్లో పని చేయడం మానివేసారా లేక పని పద్ధతులు మార్చుకున్నారా ? **[Prompt: "Work" may mean housework and chores.]**	Yes……1 No……0 → 9.3	
9.2	How have you changed your work or work schedule since you learned you were pregnant? మీరు గర్భవతి అని తెలిసినప్పటి నుండి మీరు మీ పనిని లేక పని పద్ధతులను ఎలా మార్చుకున్నారు ?	_____ _____ specify	
9.3	Do you eat any specific kinds of food to eat especially because you are pregnant? గర్భవతిగా ఉండడం వలన మీరు ఏమైనా ప్రత్యేకమైన ఆహారం తీసుకుంటారా ?	Yes……1 No……0 Don't know……..77	9.5

9.4	What kind of specific foods you eat especially because you are pregnant? మీరు గర్భవతి అయినందున ఏ రకమైన ప్రత్యేకమైన ఆహారం తీసుకుంటారు ?	_____ _____ specify	
9.5	Is there a particular food specified by your family members /community / elders/well-wishers advised you to eat during pregnancy? గర్భవతిగా ఉన్నప్పుడు మీ కుటుంబ సభ్యులు/ కులపెద్దలు/శ్రేయోభిలాషులు, ఏమైనా ప్రత్యేకమైన ఆహారమును తీసుకోమని సలహా ఇచ్చినారా ?	Yes.....1 No.....0 →	9.7
9.6	What has your family members/ community /elders/well-wishers are advised you to eat during pregnancy? మీరు గర్భవతిగా ఉన్నప్పుడు మీ కుటుంబ సభ్యులు/ కులపెద్దలు/శ్రేయోభిలాషులు, ఏ రకమైన ప్రత్యేకమైన ఆహారం తీసుకోమని సలహా ఇచ్చారు ?	_____ _____ specify	
9.7	Has your family members / community/elders/well-wishers advised you to abstain from eating certain foods because of your pregnancy? మీరు గర్భవతి అని కొన్ని పదార్థములు తినకూడదని మీ కుటుంబ సభ్యులు/కులపెద్దలు/ శ్రేయోభిలాషులు సలహా ఇచ్చినారా ?	Yes.....1 No.....0 →	9.9
9.8	What has your family members/ community /elders/well-wishers advised you to abstain from eating? ఏ పదార్థములు తినకూడదని మీ కుటుంబ సభ్యులు/ కులపెద్దలు/శ్రేయోభిలాషులు, మీకు సలహా ఇచ్చారు ?	_____ _____ specify	
9.9	Have you eaten any particular food to help with nausea during the pregnancy? మీరు గర్భవతిగా ఉన్నప్పుడు తలతిరగడం లాంటివి రాకుండా ఉండడానికి ఏమైనా ప్రత్యేకమైన ఆహారమును తీసుకున్నారా ?	Yes.....1 No.....0 →	10.1
9.10	Please describe the food you ate to help with nausea during pregnancy. గర్భవతిగా ఉన్నప్పుడు తల తిరగడం లాంటివి జరగకుండా ఉండడానికి మీరు ఏ ఆహారమును తీసుకున్నారో వివరించండి.	_____ _____ specify	

10. CIGARETTE / BIDI, CAFFEINE EXPOSURE			
Exposure to smoking from others (passive smoking)			
10.1	Since you have been pregnant, have you been exposed to tobacco smoke (like cigarette, bidi, hookah etc.) because of smoking by others? మీరు గర్భవతిగా ఉన్నప్పటి నుండి ఇతరులు పొగత్రాగడం వలన మీరు పొగాకు పొగ (అనగా సిగరెట్టు, బీడీ, హుక్కా, మొదలైనవి) పొగకి గురి అయ్యారా ?	Yes ……1 No……0 →	10.6
10.2	About how many hours per day are you exposed to this smoke because of smoking by others? మీ ఇంటిలో ఉన్న ఇతరులు పొగత్రాగడం వలన రోజుకి ఎన్ని గంటలు మీరు సిగరెట్టు/బీడీ పొగకి గురి అవుతున్నారు ?	☐☐ Hours per day	
10.3	Which of the others in your house smoke tobacco? మీ ఇంటిలో ఉన్న వారిలో ఎవరు పొగాకు త్రాగుతారు ?	Husband……A Father-in-law……B Mother-in-law……C Other person _____ D (specify)	
10.4	Prior to your pregnancy, did your husband smoke tobacco-related products (like cigarette, bidi, hookah etc.)? మీరు గర్భవతి కాక ముందు మీ భర్త పొగాకుకి సంబంధించిన పదార్థములు (అనగా సిగరెట్టు, బీడీ, హుక్కా,మొదలైనవి) త్రాగేవారా ?	Yes ……1 No……0	
10.5	Does your husband currently smoke tobacco related products ? ప్రస్తుతం మీ భర్త పొగాకుకి సంబంధించిన పదార్థములు త్రాగుతున్నారా ?	Yes ……1 No……0	
10.6	Do you chew anything on a regular basis (e.g. pan masala, betel leaves, betel nuts, tobacco) మీరు క్రమముగా వక్క, పాన్ మసాలా, తమల పాకులు, తంబాకు లాంటివి ఏమైనా నములుతారా ?	Yes……1 No……0 Did not answer……88 →	10.9
10.7	What do you chew? మీరు ఏమి నములుతారు?	Pan masala……A Betel leaves……B Betel nuts……C Tobacco……D Other_____ E (specify)	
10.8	How often do you chew? మీరు ఎంత తరచుగా నములుతారు ?	More than once a day……1 Once a day……2 Every few days……3 Once per week……4 Occasionally……5	
10.9	How many cups of chai /coffee do you drink per day? మీరు రోజుకి ఎన్ని కప్పుల 'టీ'/'కాఫీ' త్రాగుతారు?	Chai ☐☐ Cups per day Coffee ☐☐ Cups per day	END

APPENDIX C

LIFE STUDY PREGNANCY LOSS QUESTIONNAIRE

SHARE INDIA
MediCiti Institute of Medical Sciences
Ghanpur, Medchal, Ranga Reddy District-501401 A.P

LIFE PILOT STUDY 2009
Life Pilot Study Pregnancy Loss Questionnaire

IDENTIFICATION

Mandal : _____ Village : _____

Family Code : _____ Contact Tel: _____

Husband's Name : _____ Study ID: _____

Wife's Name : _____ Study ID: _____

Date of Interview : ☐☐ / ☐☐ / ☐☐☐☐
DAY MONTH YEAR

Record the Time : ☐☐ ☐☐
Hours Minutes

Interviewer's Name/ID: _____

Introduction:

Thank you, for agreeing to respond to the questions in this questionnaire. We are asking each of these questions because we believe they may play a role in determining your health and may have an influence for the loss of pregnancies. We hope that if we find out the reasons of miscarriages, that we may be able to do something in the future to make sure in avoiding the loss of pregnancies .

None of this information will be shared with anyone outside of the project. We will keep your information confidential and anonymous. If you feel uncomfortable or do not want to answer any question, please say this and I (the Interviewer) will then move to the next question. If you have any doubts about why we are asking certain questions, please ask and I will explain the reason for the question. None of the questions are meant to offend, imply anything, or make judgments about you or your family.

పరిచయం :- ఈ ప్రశ్నావళిలోని ప్రశ్నలకు సమాధానము ఇవ్వడానికి అంగీకరించినందుకు మీకు మా వందనాలు. మేము అడిగే ప్రతి విషయములు మీ ఆరోగ్యాన్ని నిర్ధారించుటలో పాత్ర వహిస్తుందని మరియు గర్భస్రావం జరగకుండా దానిని నివారించి భవిష్యత్తులో ఆరోగ్యవంతమైన గర్భం దాల్చడానికి అవకాశాలుంటాయని మేము భావిస్తున్నాము.

ఈ సమాచారము ప్రాజెక్టు బయట ఎవరితోను పంచుకోము. ఈ సమాచారము చాలా రహస్యంగా ఉంచుతాము మరియు మీ పేరు ఎక్కడా చూపము. ఒకవేళ మీకు ఇబ్బందికరంగా ఉంటే ఏదైనా ప్రశ్నకు సమాధానము ఇవ్వడం ఇష్టం లేకపోతే దయచేసి నాకు (ఇంటర్వ్యూచేయువారికి) తెలుపండి. ఒకవేళ ఈ ప్రశ్నలు ఎందుకు అడుగుచున్నారనే అనుమానం కలిగినట్లయితే దయ చేసి మమ్ము అడగండి. నేను దానికి గల కారణాలను వివరిస్తాను. ఏ ప్రశ్న కూడ మిమ్మల్ని లేక మీ కుటుంబాన్ని కించపరచడానికి లేక మీ స్థితిగతులపై తీర్పు చెప్పడం కొరకు కాదు.

1. TO BE FILLED OUT BY LIFE STUDY STAFF PRIOR TO MEETING PARTICIPANT			
1.1	Date of this pregnancy first came to know by LIFE staff. ఈ గర్భమును గూర్చి మొదటి సారిగా **LIFE** ప్రతినిధి తెలుసుకున్న తేది.	☐☐ ☐☐ ☐☐☐☐ Day Month Year	
1.2	Was a pregnancy test administered with a positive result? గర్భ పరీక్షలో గర్భము దాల్చిన విషయము నిర్ధారించబడినదా?	Yes……1 No……0	
1.3	Date pregnancy test administered with positive result. గర్భము దాల్చిన విషయము నిర్ధారించబడినతేది.	☐☐ ☐☐ ☐☐☐☐ Day Month Year	
1.4	At which visit was the pregnancy detected? గర్భవతి అని ఏ సందర్శనలో నిర్ధారించబడింది?	Registration Visit …… 1 LMP Follow-up Visit …… 2	
1.5	What is the LMP date? చివరి బహిష్టు(గత నెలసరి) తేది?	☐☐ ☐☐ ☐☐☐☐ Day Month Year	
1.6	How did LIFE staff come to know about the pregnancy loss? గర్భస్రావం జరిగిన విషయము **LIFE** ప్రతినిధులు ఎలా తెలుసుకున్నారు?	CHV reported…….. 1 Pregnancy test during 1st trimester ……. 2 Participant reported ……3 Other (Specify) _____ 4	
TO ASK THE LIFE PARTICIPANT 2. PREGNANCY LOSS QUESTIONS గర్భస్రావమునకు సంబందించబడిన ప్రశ్నలు			
2.1	Do you know when the pregnancy ended? గర్భస్రావం ఎప్పుడు జరిగిన విషయము మీకు తెలుసా? **[PROMPT: Use events of the past few months to help determine an approximate date if the participant does not know the exact date]** [గత మాసములో జరిగిన పండుగలు లేదా ముఖ్య సంఘటనలను ఉపయోగించండి]	Yes……1 No……0 → 2.3	
2.2	What was the date the pregnancy ended? గర్భస్రావం జరిగిన తేది? **[PROMPT: Record only month and year if that is all she remembers]**	☐☐ ☐☐ ☐☐☐☐ Day Month Year Don't know…… 77	

2.3	How many weeks pregnant were you when the pregnancy ended? మీకు గర్భస్రావం జరిగినపుడు మీరు ఎన్ని వారాల గర్భవతి? **[PROMPT: If the woman is unsure help her to calculate from her LMP]** [స్త్రీ కి గుర్తులేని యెడల గత నెలసరి తేది నుంచి దినములు లెక్కించడానికి సహాయపడండి]	☐☐ weeks Don't know……77	
2.4	What happened? (CIRCLE ONE, DO NOT READ RESPONSES ALOUD) ఏమి జరిగింది? (సర్కిల్ చేయండి, జవాబులు పెద్దగా చదవకండి) **[Probe: Can you briefly tell me what happened when your pregnancy ended?]** **[గర్భస్రావం జరగడానికి గల కారణాలను మీరు క్లుప్తంగా వివరించండి]**	A Miscarriage (loss of pregnancy before 20 weeks) గర్భస్రావం (20 వారాల ముందు గర్భస్రావం) …….. 1 An Ectopic or Tubal Pregnancy (pregnancy that occurs outside of the uterus, typically in the fallopian tubes) ఎక్టోపిక్ లేదా ట్యూబల్ గర్భము(గర్భము గర్భసంచి బయట ఏర్పడుట, ఫాలోపెయన్ ట్యూబ్ లో క్లిష్టముగా జరుగు వక్రియ) …….. 2 Stillbirth (delivery of a baby that was not alive at birth/loss of pregnancy after 20 weeks) మృత శిశువు (చనిపోయిన శిశువును ప్రసవించడం/20 వారాలనంతరం గర్భస్రావం జరగడం) …… 3 A Molar Pregnancy (Cyst clusters formed in uterus instead of/in addition to a fetus) మోలార్ గర్భము (గర్భసంచిలో పిండమునకు బదులుగా కంతులు తయారవుట) …….. 4 Elective abortion (Participant chose to end pregnancy) ఎలెక్టివ్ అబార్షన్ (మీ అంగీకారంతో గర్భమును తొలగించుట) …… 5 Doctor's suggestion for medical abortion based on mother's health (Doctor suggested that the participant end the pregnancy) డాక్టర్ సలహా ప్రకారం తల్లి ఆరోగ్యం స్థితిని బట్టి వైద్య పరంగా తొలగించుట (పాత్రదారికి గర్భం తొలగించాలని డాక్టర్ సలహా ఇచ్చుట)……..6 Other (Specify)_____ 10 మరియే ఇతర కారణాలు (వివరణ) Don't know……77	--> 2.6 → 2.5 2.6

2.5	Why did doctor recommend you end the pregnancy? ఏ కారణం వలన డాక్టర్ మీకు గర్భం తొలగించాలని సలహా ఇచ్చారు?	Chromosome abnormality……1 Diabetes……2 Heart disease……3 Other (specify)_____4 Don't know……77 Did not answer……88	
2.6	Did you visit a doctor/hospital or clinic at the time the pregnancy ended? గర్భస్రావం జరిగినపుడు మీరు డాక్టర్/ఆసుపత్రి లేదా క్లినిక్ ని సంప్రదించారా?	Yes……1 No……0 Don't know…… …77 Did not answer……88	→ 3.1
2.7	When did you visit the doctor/hospital/clinic? మీరు ఎప్పుడు డాక్టర్/ఆసుపత్రి లేదా క్లినిక్ ని సంప్రదించారు?	☐☐ ☐☐ ☐☐☐☐ Day Month Year Don't know…… 77	
2.8	Where did you go? మీరు ఎక్కడ సంప్రదించారు?	UHC/UHP/UFHC/CHC/PHC/SC (Public Hospital) …… A Private Clinic or Doctor's Office ……B Registered Medical Practitioner (RMP)/ Homeopath …… …..C MediCiti ……D Private Nursing Home or Private Hospital – Other than MediCiti …… E Traditional Healer …… F Some Other Place _____ G (Specify) _____ Specific name of place, and village, where went_____ Don't know/unknown …… 77 Did not answer question …… 88	
3. Prior to pregnancy loss			
3.1	Did you have any ANC check-ups? మీకు ఏమైనా ANC పరీక్షలు జరుగబడినాయా?	Yes……1 No……0	→ 3.3
3.2	Where did you go for ANC? మీరు గర్భసంరక్షణ (ANC) కొరకై ఎక్కడ సంప్రదించారు?	UHC/UHP/UFHC/CHC/PHC/SC (Public Hospital) …… A Private Clinic or Doctor's Office …… B Registered Medical Practitioner (RMP)/ Homeopath …… C MediCiti …… D Private Nursing Home or Private Hospital – Other than MediCiti …… E	

		ICDS (Anganwadi) Center …….. F Traditional Healer …….. G DAI (Traditional Birth Attendant) ……. H Some Other Place _____ I specify Specific name of place, and village, where had ANC_____ Don't know/unknown …… 77 Did not answer question …….. 88	
3.3	In the **month before the pregnancy ended**, did you suffer any of these conditions? మీకు గర్భస్రావం జరిగిన ముందు నెలలో మీరు ఏమైనా ఈ క్రింది లక్షణాలతో బాధపడ్డారా?	YES NO NO. OF DAYS ILL a. Diarrhea విరేచనాలు 1 0 ☐☐ b. Blood in stools మలములో రక్తం 1 0 ☐☐ c. Respiratory infections(cough etc) శ్వాసకోశ వ్యాధులు (దగ్గు, మొదలైనవి) 1 0 ☐☐ d. Throat infections (sore throat) గొంతు వ్యాధులు (పొడి దగ్గు) 1 0 ☐☐ e. Urinary tract infection మూత్ర సంబంధ వ్యాధి 1 0 ☐☐ **[prompt: burning, blood in urine, difficulty starting or stopping urination]** f. Fever జ్వరం 1 0 ☐☐ g. Mental stress, depression, problems with emotions మానసిక ఒత్తిడి, క్రుంగి పోవుట, భావోద్రేక సమస్యలు 1 0 ☐☐ h. Any accident (car accident, fall) happened? ఏదైనా ప్రమాదము జరిగిందా? 1 0 ☐☐	
3.4	In the **month before the pregnancy ended**, did you take any antibiotic or medication or pills or injection for any infection? గర్భస్రావం జరిగిన ముందు నెలలో మీరు ఏదైనా ఇన్ఫెక్షన్ కొరకు ఆంటీబయాటిక్ మందులు లేక సూదులు తీసుకున్నారా?	Yes……1 No……0 Don't know……..... …77 Did not answer……...88	3.6

3.5	*Interviewer should first write down any medications to be coded later as antibiotics* ఇంటర్ వ్యూ చేయువారు మందు పేరు ఒక ప్రక్కన వ్రాసుకోవాలి. తరువాత అవి ఆంటీబయాటిక్ మందులో కావో కోడ్ చేసుకోవాలి	Medications (specify) Days Taken 1_____ ☐☐ 2_____ ☐☐ 3_____ ☐☐ 4_____ ☐☐	
3.6	**In this section I am asking about vitamin deficiencies. When someone is missing certain vitamins in their diets there are three things they might experience:** **very sore and swollen tongue;** **cracks and soreness at the corners of the mouth;** **Night blindness.** **These symptoms of vitamin deficiency would last a long time, difficult to treat, and would probably get worse over time before getting better.**		
	From the beginning of the pregnancy, have you had sore tongue, cracks at the corners of the mouth, night blindness that lasted more than a week and got worse over time? మీరు గర్భవతి అని నిర్ధారణ జరిగిన తరువాత మీరు ఎప్పుడైనా నాలుకపై పుండ్లు, పొక్కులు లేక రేచీకటి లాంటి లక్షణాలతో వారం కన్నా ఎక్కువ కాలం భాధపడ్డారా? a. Sore tongue నాలుకపై పొక్కులు b. Cracks at the corners of the mouth నోటి చివరిలో పగుళ్ళు/పొక్కులు c. Night blindness రేచీకటి	YES NO MEDICATION 1 0 [_____] 1 0 [_____] 1 0 [_____]	
3.7	Before the pregnancy ended, did you have any vaginal bleeding? గర్భస్రావం జరగక మునుపు మీకు రక్తస్రావం ఏమైనా జరిగినదా?	Yes……..1 No……..0 Don't know……..…77 Did not answer……...88	3.9
3.8	How many pads/cloths did you use for the bleeding at its heaviest? మీకు రక్తస్రావం (ఎరబట్ట) ఎక్కువగా అయినపుడు మీరు రోజుకి ఎన్ని ప్యాడ్ లు /బట్టలు వాడారు?	Spotting ……..…..…….. 1 1-2 pads per day……... 2 3-4 pads per day ……...……3 >4 pads per day ……..…..... 4 1-2 cloths per day ……..…….. 5 3-4 cloths per day ……..…… 6 >4 cloths per day ……..…….. 7 Don't know……..…….. 77 Did not answer……..…… 88	

3.9	**[Prompt: If the participant did not see a health care provider during their pregnancy, skip to Question #4.1.]** **During the pregnancy** were you **told by a doctor or other health care provider** that you had any of the following conditions? మీరు గర్భవతిగా ఉన్నప్పుడు మీకు డాక్టర్ లేదా ఆరోగ్య సంరక్షులు ఈ క్రింది వాటిలో ఏమైనా ఉన్నాయని చెప్పినారా?			
		YES	NO	DON'T KNOW
	a. Sugar Disease షుగర్ వ్యాధి	1	0	77
	b. High Blood Pressure అధిక రక్తపోటు	1	0	77
	c. Swelling of your feet పాదాల వాపు	1	0	77
	d. Swelling of your face ముఖం వాపు	1	0	77
	e. Contractions of your uterus గర్భకోశంలో కాంట్రాక్షన్స్ రావడం	1	0	77
	f. Very sore throat for several days or more చాలా రోజులుగా గొంతు నొప్పి	1	0	77
	g. Anemia రక్త హీనత	1	0	77
	h. One or more sores on your genitals యోని వద్ద ఒకటి లేక ఎక్కువ కురుపులు	1	0	77
	i. A vaginal discharge యోని స్రావము	1	0	77
	j. Diarrhea నీళ్ళ విరేచనాలు	1	0	77
	k. Jaundice పసికర్లు	1	0	77
	l. Burning or pain when you urinate మూత్రం పోసేటప్పుడు నొప్పి లేక మంట	1	0	77
	m. Goiter గొంతులో కణితి	1	0	77
	n. Any other pregnancy related condition ఇంకా ఏదైన గర్భధారణకి సంబందించిన బాధ _____ Specify	1	0	77

THANK THE RESPONDENT FOR HER CO-OPERATION AND REASSURE HER ABOUT THE CONFIDENTIALITY OF HER ANSWERS

RECORD THE TIME:_____ Hour ☐☐
Minutes ☐☐

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